FINAL REPORT

Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 to 52/53

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(Component 1)

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October 7, 2002 - October 22, 2003
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ABSTRACT

The Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), assembled by the U.S. Environmental Protection Agency (EPA) in 1996, recommended the use of a male 20-day pubertal assay with thyroid assessment to evaluate test materials that are only effective orally, or after a dosing duration longer than that used in the uterotrophic assay (EDSTAC Report, 1998). This assay is the most comprehensive assay in the proposed Tier 1 battery of optional assays. It is capable of detecting substances that alter thyroid function, that are aromatase inhibitors, estrogens, anti-estrogens, androgens, and anti-androgens, and that interfere with the hypothalamus-pituitary-gonadal or –thyroid axis. Although the experiments completed or in progress are believed to be sufficient to demonstrate the usefulness of the female pubertal assay for a wide variety of chemicals, EPA felt that additional multiple-dose studies across an array of chemicals would provide greater confidence in the reliability and relevance of the assay. Therefore, EPA decided to test eight additional chemicals that have various modes of action, i.e., atrazine, p, p'-dichlorodiphenyldichloroethylene (p, p'-DDE), vinclozolin, methoxychlor, propylthiouracil, ketoconazole, linuron, and phenobarbital using the male pubertal assay.

The study was conducted in two components. In each component, F1 males, produced from undosed timed-pregnant CD® (Sprague-Dawley) rats (the F0 generation), were used. On the day of birth (pnd 0), F1 pups were counted, sexed, weighed, and examined externally. On pnd 4, the litters were standardized to ten pups, maximizing the number of male pups. Natural litters with ten or fewer pups were not culled. The F0 females were allowed to rear their pups to pnd 21. F1 survival, gender identification, gross observations, and body weight were recorded on pnd 4, 7, 14, and 21. On pnd 21, F1 males were weaned and weight ranked across litters, then randomized into the treatment groups based on body weight. Fifteen F1 males were assigned to each treatment group in each component. F1 males were orally dosed with a test compound or the vehicle (corn oil) from pnd 23 to pnd 52/53. Dose volume (5 ml/kg/day) was based on daily body weight. In Component 1, animals received atrazine (75 or 150 mg/kg/day), p, p'-DDE (50 or 100 mg/kg/day), vinclozolin (30 or 100 mg/kg/day) or methoxychlor (25 or 50 mg/kg/day) in Mazola® corn oil. In Component 2, animals received propylthiouracil (2 or 25 mg/kg/day), ketoconazole (50 or 100 mg/kg/day), linuron (50 or 100 mg/kg/day), or phenobarbital (50 or 100 mg/kg/day) in Mazola® corn oil. A separate vehicle control group dosed with corn oil was run

concurrently with each component. Daily body weights and feed consumption for the F1 males were recorded during the post weaning treatment period to scheduled sacrifice. Clinical signs were recorded twice daily during the treatment period. Beginning on pnd 23, F1 males were examined for preputial separation; the day of complete preputial separation was identified as the age of acquisition of preputial separation.

At necropsy on pnd 52/53, the males were euthanized, and blood was collected by external cardiac puncture for analysis of thyroxine (T4) and thyroid-stimulating hormone (TSH). Body and organ weights were recorded. The testis, epididymis, and thyroid were evaluated histopathologically. The following observations were made:

- **Atrazine**. Treatment with atrazine at 75 or 150 mg/kg/day did not affect the day of acquisition of preputial separation. Adjusted organ weights exhibited an increasing trend for paired testes weight. No differences were noted in T4 or TSH levels, and no treatment-related histopathological changes were observed in the thyroid, testes, or epididymides.
- **p,p'-DDE.** Treatment with 50 or 100 mg/kg/day p,p'-DDE significantly delayed preputial separation at both treatment levels. Adjusted thyroid, liver, and paired kidney weights were significantly increased at both doses of p,p'-DDE. With respect to reproductive tissues, adjusted paired epididymides weight exhibited a significant decrease at the high dose, and levator ani plus bulbocavernosa muscle complex (LABC) weight exhibited a decreasing trend. Decreased T4 was observed at the high dose, whereas TSH was not significantly affected.
- **Vinclozolin**. The day of preputial separation exhibited significant delays at both the 30 and 100 mg/kg/day dose levels. In addition, two males in the high-dose group failed to achieve preputial separation prior to scheduled necropsy. Adjusted weight of paired testes (increase), paired epididymides (decrease), and paired seminal vesicles with coagulating glands (decrease) exhibited significant treatment-related effects at both dose levels. Adjusted dorsolateral and total prostate, and LABC weight exhibited a significant decrease at the high dose. T4 levels were significantly decreased at both doses of vinclozolin, while no effect was observed on TSH.
- **Methoxychlor.** No effect on preputial separation was noted at either 25 or 50 mg/kg/day methoxychlor. Adjusted paired adrenal weight (increase) and seminal vesicle with coagulating glands (decrease) exhibited a significant difference from the control group, and only at the high dose. Thyroid hormones were unaffected, and no treatment-related histopathology was observed.
- **Propylthiouracil.** As expected, propylthiouracil produced a decrease in T4 and an increase in TSH, increased adjusted thyroid weight, and thyroid follicular cell hypertrophy/hyperplasia at both 2 and 25 mg/kg/day. Preputial separation was significantly delayed at the high dose. Treatment effects were also observed at both doses in the increased adjusted weights of the seminal vesicles with coagulating glands. Adjusted liver weight and paired epididymides weight exhibited an increasing trend.
- **Ketoconazole.** The postnatal day of acquisition of preputial separation was delayed at both doses of ketoconazole. Other treatment-related changes observed at both treatment levels included increased adjusted liver and paired adrenal weight, and decreased adjusted seminal vesicles with coagulating glands weight. The high dose of ketoconazole

also increased adjusted paired kidney weight and decreased adjusted paired testes weight. No effect of treatment was observed histologically in the testes, epididymides, or thyroid. Thyroid hormone levels were not affected.

- **Linuron.** Linuron delayed puberty at both the 50 and 100 mg/kg/day dose levels, as evidenced by delayed acquisition of preputial separation. Adjusted liver weight exhibited a treatment effect (increase) at both dose levels; adjusted seminal vesicles with coagulating glands weight was decreased at the high dose. Both T4 and TSH levels were decreased at both dose levels, although the decrease in TSH at the high dose of linuron did not reach statistical significance.

- **Phenobarbital.** The postnatal day of acquisition of preputial separation was delayed at both doses of phenobarbital. In addition, treatment-related effects were detected at both dose levels in an increase in the adjusted weights of the thyroid and liver. A decrease in adjusted organ weight was observed at the high dose for paired testes and LABC. Adjusted paired epididymides weight exhibited a decreasing trend. No effect of treatment was observed on circulating T4 or TSH levels, or histologically in the testes, epididymides, or thyroid.

OBJECTIVE

The objective of this study was to examine the sensitivity of the male pubertal assay to the effects of a wide variety of chemicals that are known to affect the endocrine system through different pathways and/or mechanisms of action. This assay is the most comprehensive assay in the proposed Tier 1 battery of assays, as it is capable of detecting substances that alter thyroid function, that are aromatase inhibitors, estrogens, androgens, antiandrogens, and thyroid-active compounds that are agents which interfere with the hypothalamus-pituitary-gonadal axis. Results from other shorter assays and/or with the use of intraperitoneal (i.p.) injection as the route of administration, have also been reported (O'Connor et al., 1998a,b; 1999a,b; 2000a,b; 2002a,b). Although the experiments that have been completed or in progress are believed to be sufficient to demonstrate the usefulness of these pubertal assays for a wide variety of chemicals, EPA felt that additional multiple-dose studies across an array of chemicals would provide greater confidence in the reliability and relevance of the female pubertal assay. Therefore, EPA decided to test eight additional chemicals that have various modes of action.

MATERIALS AND METHODS

Test Materials and Dose Formulations

The test chemicals were procured and analyzed for purity by the sponsor, by means of gas chromatography with a flame ionization detector (GC-FID), gravimetric analysis, or high performance liquid chromatography (HPLC), as indicated below. For atrazine, characterization was conducted on one lot, whereas dosing was accomplished with two lots, as indicated below. All bulk test chemicals were stored at Battelle, at room temperature, with the exception of phenobarbital, which was stored at 4°C.

Atrazine

CAS Number:	1912-24-9
Supplier:	Chem Services
Lot No. (Characterization):	277-93B
Purity (Battelle):	99.9% (GC-FID)
Lot Nos. (dosing):	289-102A and 285-63B (not characterized)

p, p-DDE

CAS Number:	72-55-9
Supplier:	Aldrich
Lot. No.:	09020KU
Purity (Battelle):	99.4% (GC-FID)

Vinclozolin

CAS Number:	50471-44-8
Supplier:	Chem Services
Lot No:	281-94A
Purity (Battelle):	99.7% (GC-FID)

Methoxychlor

CAS Number:	72-43-5
Supplier:	Sigma
Lot No.:	049H1328
Purity (Battelle):	89.7% (GC-FID)

Propylthiouracil

CAS Number:	51-52-5
Supplier:	TCI
Lot. No.:	GB01
Purity (Battelle):	99.9% (gravimentric)

Ketoconazole

CAS Number:	65277-42-1
Supplier:	Spectrum Laboratory Products
Lot. No:	QL0352
Purity (Battelle):	100% (HPLC)

Linuron

CAS Number:	330-55-2
Supplier:	Chem Services
Lot Number:	273-81B
Purity (Battelle):	99.5 (HPLC)

Phenobarbital

CAS Number:	50-06-6
Supplier:	Sigma
Lot Number:	81K2620
Purity (Battelle):	99.1% (HPLC)

Mazola® corn oil (expiration dates 4-03, 9-03, 12-03 and 1-04) was purchased by Battelle-Sequim from retail outlets. Peroxide determination of the corn oil used was 2.07 meq/kg (expiration date 4-03), 1.38 meq/kg (expiration date 9-03), 1.77 meq/kg (expiration date 12-03), and 1.34 meq/kg (expiration date 1-04). The corn oil was stored in the freezer. Test chemicals formulated in corn oil were stored at 4°C. Dose formulations were mixed in corn oil for administration at 5 ml/kg. One vehicle formulation was mixed to be administered to the control group animals assigned to Component 1

compounds, whereas a separate vehicle formulation was mixed to be administered to the control group animals assigned to Component 2.

Stability analysis conducted at Battelle-Sequim, of test dose formulations of each chemical in corn oil indicated that the formulations were stable for at least eight weeks, with the exception of p, p'-DDE, and methoxychlor, which were stable for at least 6 and 4.5 weeks, respectively. Formulations assayed (triplicate average) between 91.0% and 109.6% of the target concentration prior to shipping to RTI International (Tables 1-A through 1-H). Additional information may be found in Appendix III (Final Chemical Reports for WA 2-14, Battelle, July 24, 2003).

Animals and Husbandry

For Component 1, 20 timed-pregnant and 2 nonpregnant female outbred albino CD® (Sprague-Dawley) rats (Crl:CD®[SD] IGS BR) were received from Charles River Breeding Laboratories (Raleigh, NC) on September 5, 2002 at gestational day (gd) 13 (Table 1). A separate order of 20 timed-pregnant and 2 nonpregnant female rats were received on December 26, 2002 for use in Component 2. The females were 10 weeks old upon arrival at RTI.

Table 1. Study Schedule

Event	Dates
Component 1 (Atrazine, DDE, Vinclozolin Methoxchlor)	
Receive 20 females at gd 13	September 5, 2002
Quarantine (gd 13-20)	September 5–12, 2002
pnd 0	September 14-16, 2002
pnd 21	October 5-7, 2002
1st day of dosing (pnd 23)	October 7-9, 2002
Necropsy (pnd 52/53)	November 5-7, 2002
Component 2 (Propylthiouracil, Ketoconazole, Linuron, Phenobarbital)	
Receive 20 females at gd 13	December 26, 2002
Quarantine (gd 13-20)	December 26 – January 2, 2003
pnd 0	January 4, 5, 2003
pnd 21	January 25, 26, 2003
1st day of dosing (pnd 23)	January 26, 2003
Necropsy (pnd 52/53)	February 26, 27, 2003
Reproductive Organ/Thyroid Histopathology complete	October 22, 2003
Hormone Analysis Complete	May 20, 2003

For each component, the animals were quarantined for one week, during which time they were weighed and examined by a veterinarian. Representative animals were subjected to fecal examination. Within one day after receipt of each shipment, the two nonpregnant female rats were sacrificed and blood

collected for assessment of viral antibody status. Heat-inactivated serum was sent to BioReliance (Rockville, MD) for their Level 1 Rat Antibody Screen. The viral screen consisted of evaluation for the presence of antibodies against the following:

- Toolan H-1 virus (H-1),
- Sendai virus,
- pneumonia virus of mice (PVM),
- rat coronavirus/sialodacryoadenitis (RCV/SDA),
- Kilham rat virus (KRV),
- CAR *Bacillus* (CARB),
- *Mycoplasma pulmonis* (*M. Pul.*), and
- parvo (PARVO).

Results of the physical examination, serology, and parasitology were negative for signs of infectious disease. The animals were considered to be in good health and suitable for use in this study.

The experiment was carried out under standard laboratory conditions. The F0 animals were individually housed during the quarantine period and during gestation, and with their litters in solid-bottom polycarbonate cages with stainless-steel wire lids (Laboratory Products, Rochelle Park, NJ) with Sani-Chip® cage litter (P.J. Murphy Forest Products Corp., Montville, NJ). Postwean retained F1 males were housed singly until necropsy. All animals were housed in the RTI Animal Research Facility for the duration of the study. Due to an oversight, Room 201 was on a 12:12 (light:dark) light cycle for the first 30 days of the study. Thereafter, all animal rooms were on a 14:10 hour (light:dark) light cycle per day and were air-conditioned; temperature and relative humidity (RH) were continuously monitored, controlled, and recorded using an automatic system (Siebe/Barber-Colman Network 8000 System, Version 4.4.1, Loves Park, IL). The protocol-mandated temperature range was 64 to 79°F (18-26°C), and the RH range was 30-70% (NRC, 1996). The F0 and F1 animals (prior to weaning) in Component 1 were housed in Room 201 of the Animal Research Facility. Temperature and RH readings for the animal rooms, excluding transient deviations (as noted in the Protocol Deviation list, page 36) are presented here. Temperature and RH readings for Room 201 from September 5 to October 6, 2002, were 70.2 to 74.2°F and 44.5% to 62.6% RH. F1 animals were housed in Room 303 after weaning. Temperature and RH readings for Room 303 from October 5 to November 7, 2002, were 70.5 to 77.9°F and 45.8% to 61.4% RH. F0 and F1 animals in Component 2 were housed in Room 403 from December 26, 2002 to February 27, 2003. Temperature and RH readings for Room 403 from December 26, 2002 to February 27, 2003 were 70.2 to 73.3°F and 33.7 to 60.6% RH.

Purina Certified Rodent Chow (No. 5002, PMI Feeds, Inc., St. Louis, MO; batch numbers documented in the study records) was available *ad libitum*. The metabolizable energy content for this feed is 3.10 kcal/gm. All animals in all groups received either batch/lot #JUN 24 02 1B or #DEC 02 02

2B of Purina Certified Rodent Chow. The analyses of each feed batch for nutrient levels and possible contaminants were performed by the supplier, examined by the Study Director, and maintained in the study records. The feed was also analyzed at the manufacturer for the phytoestrogens (isoflavones) daidzein, genistein, and glycitein. Analysis indicated that the total phytoestrogens (as aglycones) in these lots of feed ranged from 271 to 353 ppm (Appendix IV).

Deionized water (generated in-house from tap water; source: City of Durham, Department of Water Resources, Durham, NC) was available *ad libitum* by plastic water bottles with butyl rubber stoppers and stainless-steel sipper tubes. Contaminant levels of the Durham City water were measured at regular intervals by the supplier per EPA specifications. The deionized water was analyzed by Balazs Analytical Laboratories, Inc. (Sunnyvale, CA). There were no known contaminants that may have affected the outcome of this study. F0 females were individually identified by eartag. F0 females were allowed to give birth and rear their litters. Litters were adjusted on pnd 4 to 10 pups, maximizing the number of male pups.

After selection of the F1 male weanling study animals, four unselected male rats were designated as sentinels and eartagged. They were singly housed in the study room(s) in polycarbonate solid-bottom cages with bedding and provided feed and water *ad libitum* (as described above for study animals). They were examined once daily by cage-side observation for morbidity or mortality at the same time as clinical observations or morbidity/mortality checks for the study animals. No sentinels exhibited any morbidity or mortality. At the time of necropsy of retained F1 males, the sentinels were terminated, blood samples collected, and serum samples prepared. All sentinel serum samples were submitted to BioReliance (Rockville, MD) for serological evaluation (see above). Analysis of serum (as described above) from sentinels sacrificed during the necropsy of the retained F1 male necropsy was negative for viral antibodies.

A total of 15 F1 males per group were assigned to each component in this study. F1 males were assigned to treatment groups by stratified randomization for body weight on pnd 21, so that mean body weight on pnd 21 did not differ among treatment groups. Selected male F1 weanlings were identified by eartag, and F1 pups prior to weaning were not uniquely identified. The method and numbers for identification were documented in the study records.

All adult animals assigned to the study were euthanized by CO_2 asphyxiation. F1 pups culled on pnd 4 were sacrificed by decapitation. F0 females received with the initial shipments, but not assigned to the study, were removed from the study room when the F0 females were released from quarantine and euthanized by CO_2 asphyxiation. Similarly, F1 males not assigned to treatment groups or chosen as sentinels were removed from the study room prior to initiation of dosing and euthanized by CO_2 asphyxiation. Records were kept documenting the fate of all animals in the study.

Study Design

A graphic representation of the component study design is presented in Figure 1. The study began with 20 timed-mated females in each component.

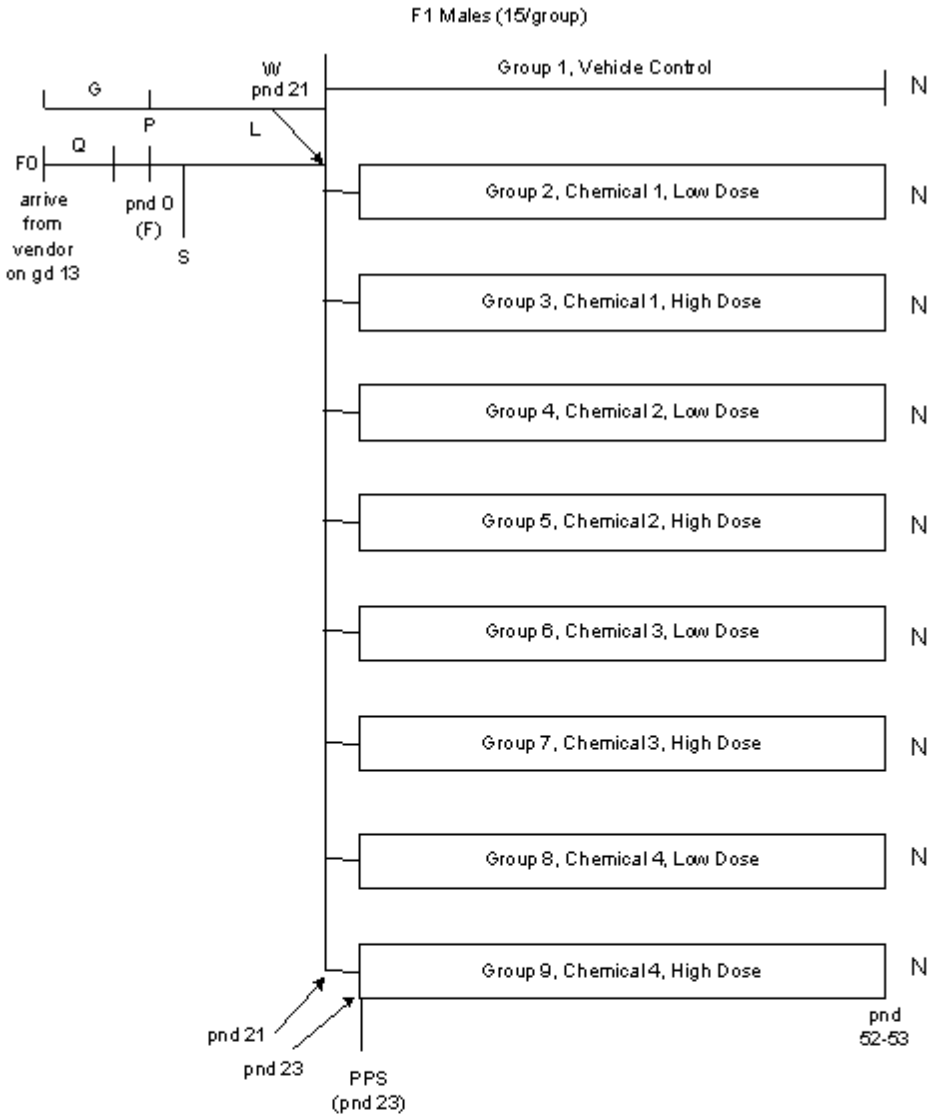

Figure 1. General Component Study Design for the Male Pubertal Assay

F0 Females

Beginning on gd 20, each female was examined twice daily (a.m. and p.m.) for evidence of littering. Females who were littering at morning and afternoon checks had this information recorded on the gestational sheet. Signs of dystocia or other signs of difficulty at parturition were also recorded, if observed. Dams that did not produce a litter by calculated gd 26 were euthanized by CO_2 and discarded. Any dams whose whole litters were born dead or died prior to pnd 21 were sacrificed, and the number of uterine implantation scars recorded. On pnd 21 of each F1 litter, each F0 dam was euthanized by CO_2 asphyxiation, and the carcass discarded. Final disposition of each animal was clearly documented in the study records.

Progeny (F1)

All pups were counted, sexed, weighed, and examined as soon as possible on the day of birth (designated as pnd 0) to determine the number of viable and stillborn members of each litter. Thereafter, litters were evaluated for survival, sex, gross observations, and body weights on pnd 4, 7, 14, and 21. Any pup which appeared moribund or died during lactation was necropsied, when possible, to investigate the cause of death and discarded. No organs were weighed or saved. On pnd 4, the size of each litter was adjusted to ten pups, maximizing the number of male pups retained. Natural litters with ten or fewer pups were not culled. All culled pups were sacrificed by decapitation. The F0 dams were allowed to rear their remaining F1 young to pnd 21. On pnd 21, each litter was weaned.

F1 Males

When each F1 litter reached pnd 21, the F1 males from each pnd 21 (wean) date were weight ranked across litters (outliers, i.e., heaviest and lightest pups, were eliminated from selection). The selected males were eartagged and distributed across the groups in each component by stratified randomization (e.g., one of the heaviest selected males went into each of the treatment groups, etc.). Of the remaining F1 males, four were eartagged and selected as sentinels.

Beginning on pnd 23, each F1 male was dosed with one of the test materials at one of the dose levels or the vehicle control (corn oil for all chemicals), as shown in Table 2. EPA selected nine test chemicals for this evaluation and selected the low- and high-target doses (in mg/kg/day) for each of them. One chemical selected for testing, finasteride, an inhibitor of a 5 α-reductase which catalyzes the conversion of testosterone to its potent metabolite, dihydrotestosterone [DHT]), could not be obtained from the manufacturer in time to be included in the study, and was eliminated from this study. The remaining eight test chemicals and their target/mechanism of action are as follows: (1) atrazine (affects the hypothalamus-pituitary axis); (2) p, p'-DDE (stable metabolite of DDT; anti-androgen through

competitive binding to the androgen receptor); (3) vinclozolin (metabolites M1 and M2 act as anti-androgens; competitive binding to androgen receptor; M1 also binds weakly to the rat progesterone receptor); (4) methoxychlor (a xeno-estrogen through α-estrogen receptor, anti-estrogen through β-estrogen receptor and an anti-androgen through androgen receptor-mediated mechanism); (5) propylthiouracil (affects the thyroid directly, causing hypothyroidism); (6) ketoconazole (inhibits steroidogenesis in both sexes); (7) linuron (anti-androgen; competitive binding to androgen receptor); and (8) phenobarbital (induces P450 isoforms predominantly in the liver, accelerates metabolism of endogenous hormones and exogenous xenobiotics). Each animal was weighed every day prior to treatment and the body weight recorded. Treatments were administered daily by oral gavage using an 18-gauge gavage needle (1 inch length with 2.25 mm ball) and a 1 cc glass or plastic (disposable) tuberculin syringe for each treatment, from pnd 23 and continuing to pnd 52/53. This duration of treatment was required for the detection of pubertal delay and antithyroid effects. Test chemicals were administered in corn oil vehicle at a dosing volume of 5 ml/kg body weight. The treatments were administered on a mg/kg body weight basis, adjusted based on the most recent body weight, and the volume of the dose administered was recorded each day.

Clinical observations of F1 male study animals were documented at least once daily on pnd 21 and 22 (prior to dosing period) and at least twice daily, at dosing and one to two hours postdosing, throughout the dosing period (pnd 23 to pnd 52 or 53). All F1 males were weighed in the morning on pnd 21 and 22, and every day in the morning during the dosing period on pnd 23 to pnd 52/53, for adjustment of dosing volume based on the most recent body weight. Daily body weights were reported and statistically analyzed. F1 male weight gains were calculated and analyzed for pnd 21-23, 23-30, 30-37, 37-44, 44-51, 51-52, 51-53, and 23-52/53 (treatment period). F1 male body weights were also recorded on the day of acquisition of preputial separation. Feed weights for the individually-housed F1 weanling males were recorded daily and reported as g/day and as g/kg body weight/day.

Beginning on pnd 23, each F1 study male was examined daily for preputial separation. The appearance of partial and complete preputial separation or a persistent thread of tissue between the glans and prepuce was recorded if it occurred. In addition, the body weight at complete preputial separation was recorded.

Necropsy for pnd 52/53 F1 Males

Blood Collection and Hormone Assays

At scheduled necropsy of the F1 males, after terminal anesthesia (CO_2 asphyxiation), the males were weighed and the maximum amount of blood was taken by external cardiac puncture and placed in a labeled tube. The blood was allowed to clot and centrifuged under refrigeration at approximately 1200 ×

g for approximately 10 minutes. The resulting serum was subdivided into three aliquots and frozen at least -20°C. One aliquot from each animal was analyzed for T4 and the second aliquot was analyzed for TSH. The remaining serum was frozen and delivered to Dr. Ralph Cooper at the U.S. EPA's National Health and Environmental Effects Research Laboratory (NHEERL) (RTP, NC).

Table 2. Study Design, Test Chemicals, and Target Doses

Group No.	No. F1 Males	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)	Dose Volume (ml/kg)
			COMPONENT 1		
1	15	[a]	0	0.0	5
2	15	Methoxychlor	25	5.0	5
3	15		50	10.0	5
4	15	Atrazine	75	15.0	5
5	15		150	30.0	5
6	15	p,p'-DDE	50	10.0	5
7	15		100	20.0	5
8	15	Vinclozolin	30	6.0	5
9	15		100	20.0	5
			COMPONENT 2		
1	15	[a]	0	0.0	5
2	15	Propylthiouracil	2	0.4	5
3	15		25	5.0	5
4	15	Linuron	50	10.0	5
5	15		100	20.0	5
6	15	Ketoconazole	50	10.0	5
7	15		100	20.0	5
8	15	Phenobarbital	50	10.0	5
9	15		100	20.0	5

[a] Corn oil, vehicle control

All assays were counted in a Packard Biosciences Cobra II Series Model 5002 gamma counter using RIASMART software (Version 1.0). The rat thyroid stimulating hormone (rTSH) RIA used was a no-extraction, double antibody ^{125}I RIA (Amersham Biosciences, Piscataway, NJ) which utilized rTSH antibody, ^{125}I-rTSH, rTSH calibrators as the standard curve, and a solution consisting of donkey anti-rabbit serum coated onto magnetizable polymer particles. Normal control serum from the same species/strain/sex as the unknown samples was also assayed. From the control values, the intra and inter-assay coefficient of variation, percent recovery, and index of parallelism for the assays were determined

(see Table 3). The sensitivity of this assay was 0.5 ng/tube. For the RIA procedure, the sample was pipetted into a glass culture tube. The rTSH antiserum was added, followed by the ^{125}I-rTSH, and the tubes were vortexed and incubated at room temperature for 20-24 hours. After overnight incubation, the anti-rabbit serum was added and the tubes vortexed. The tubes were centrifuged, the supernatant was decanted, and the tubes containing pellets were counted in a gamma counter. Results were reported as ng/ml.

The T4 RIA used was a no-extraction, solid-phase ^{125}I RIA which utilized T4-specific antibody-coated tubes and ^{125}I-T4 (DPC, Los Angeles, CA). The T4 (Sigma, St. Louis, MO) standard curve was prepared in RIA Buffer I (0.01 M sodium phosphate plus 0.85% [w/v] sodium chloride with 0.1% [w/v] sodium azide and 1% [w/v] bovine serum albumin, pH 7.6). T4 controls were prepared in the same matrix as unknown samples by adding known concentrations of T4 to male serum, as appropriate. From the control values, the intra- and interassay coefficient of variation, percent recovery, and index of parallelism for the assays were determined (see Table 3). The sensitivity of this assay was 0.25 µg/dL. For the RIA procedure, the sample was pipetted into the antibody-coated tube. The ^{125}I-T4 was added, and the tubes were vortexed and incubated in a 37°C water bath for one hour. After incubation, the supernatant was aspirated and the tubes were counted in a gamma counter. Results were reported as µg/dL.

Table 3. Characteristics of Endocrine Radioimmunoassays

	Hormone Assay	
Parameter	**T4 (µg/dL)**	**rTSH (ng/ml)**
Matrix	pubertal male serum	pubertal male serum
Intra-assay Variation:[a]		
blank matrix	0/3.8%	0/5.3%
mass added	2/3.3%	8/3.5%
	10/2.8%	32/6.1%
Interassay Variation:[a]		
number of assays	3	5
blank matrix	0/5.4%	0/10.4%
mass added	2/8.9%	8/9.9%
	10/3.4%	32/13.1%
% Recovery of Added Mass[b]	2/(61.0% - 83.0%)	8/(88.8% - 122.4%)
	10/(73.2% -77.3%)	32/(105.0% - 142.1%)
Index of Parallelism[c]	2/100.5%[d]	0/110.2%
	10/103.1%[d]	8/106.2%
		32/94.0%

[a] Numbers are concentration of mass added/percentage variation. For intra-assay variation, the number of samples assayed was ten in each case.

[b] Numbers are concentration of mass added/percentage recovered (range of all assays).

[c] Index of parallelism = concentration of low volume ÷ concentration of high volume x 100.

[d] All study samples assayed at same volume.

Gross Examination, and Histopathology

Once each F1 male was bled, the animal was necropsied and internal thoracic and abdominal organs and cavities examined. Any abnormalities were documented. The following organs were dissected out and weighed: paired testes, paired epididymides, prostate (intact and separated into ventral and dorsolateral lobes), seminal vesicles with coagulating glands (and fluid), levator ani plus bulbocavernosus muscle complex, liver, paired kidneys, adrenal glands (paired), pituitary, and thyroid (taken with attached portion of trachea, weighed after fixation and removal of the tracheal portion).

Tissues taken at necropsy were placed in fixative and then transferred to Experimental Pathology Laboratories (EPL) for processing. The testes and epididymides from each F1 male were placed in Bouin's fixative for 24 hours, after which they were rinsed and stored in 70% alcohol until embedded in paraffin. The thyroid with attached portion of trachea was fixed in 10% neutral buffered formalin. These tissues, in fixative were transferred to EPL. The thyroid was dissected and weighed at EPL. The tissues were embedded in paraffin, then sectioned at 3-5 microns and stained with hematoxylin and eosin (H and E) for subsequent histological evaluations. Optional tissues for histopathology, including the liver, paired kidneys, adrenal glands (paired) and pituitary (if warranted by organ weight change of "significant magnitude"), which were placed in 10% neutral buffered formalin, have not been processed. Stained sections were evaluated by a Board AVCP Certified veterinary pathologist (EPL) for pathologic abnormalities and potential treatment-related effects. Thyroids were evaluated for morphologic changes such as altered follicular epithelial height, the relative number and staining characteristics of colloid, the extent of thyroid vascular supply, and the density, size, and shape of the thyroid follicles. The testes and epididymides for each male were evaluated for spermatogenesis, spermiogenesis, status of seminiferous tubules in the testis, and sperm in the epididymis, as well as the structural integrity of these organs.

Statistical Analyses

All data for a single chemical (two doses) and concurrent vehicle control group were analyzed using either parametric ANOVA under the standard assumptions or robust regression methods (Zeger and Liang, 1986; Royall, 1986; Huber, 1967) which do not assume homogeneity of variance or normality. The homogeneity of variance assumption was examined via Levene's test (Levene, 1960). If Levene's test indicated lack of homogeneity of variance ($p<0.05$), robust regression methods were used to test all treatment effects. The robust regression methods use variance estimators that make no assumptions regarding homogeneity of variance or normality of the data. They were used to test for linear trends across dose as well as overall treatment group differences (via Wald chi-square tests). Significant overall treatment effects were followed by single degree-of-freedom *t*-tests for exposed vs. control group comparisons, if the overall treatment effect was significant. If Levene's test did not reject the hypothesis of homogeneous variances, standard ANOVA techniques were applied for comparing the treatment groups. The GLM procedure in SAS® Version 8 (SAS Institute, Inc., 1999a,b,c,d,e; 2000) was used to test for linear trend, evaluate the overall effect of treatment and, when a significant treatment effect is present, to compare each exposed group to control via Dunnett's test (Dunnett, 1955, 1964). Standard

ANOVA methods, as well as Levene's test, were available in the GLM procedure of SAS®, and the robust regression methods were available in the REGRESS procedure of SUDAAN® Release 7.5.4 (Shah et al., 1997) or Release 8.0 (RTI, 2001). Organ weights were also analyzed by Analysis of Covariance (ANCOVA) using body weight at necropsy as the covariate. When statistically significant effects were observed, treatment means were examined further using LSMeans. The unit of comparison was the weanling F1 male offspring on study.

A test for statistical outliers was performed in the UNIVARIATE procedure of SAS® Version 8 (SAS Institute, Inc., 1999a,b,c,d,e; 2000) on F1 male body and organ weights. If examination of pertinent study data did not provide a plausible biologically sound reason for inclusion of the data flagged as "outlier," the data was excluded from summarization and analysis and was designated as outliers. For all statistical tests, $p \leq 0.05$ (one- or two-tailed) was used as the criterion for significance.

Personnel

This study was conducted at RTI International, Research Triangle Park, NC, under contract to Battelle, Columbus, OH. Dr. David P. Houchens, EDSP Program Manager, was the Sponsor's Representative. Dr. R.W. Tyl served as Project Toxicologist. Dr. Julia D. George served as Study Director. Reproductive and Developmental Toxicology personnel included Ms. M.C. Marr (Laboratory Supervisor), Ms. C.B. Myers (Reproductive Toxicity Supervisor and Data Analyst), Mr. W.P. Ross, Ms. M.C. Rieth, Ms. V.I. Wilson, Ms. L.B Pelletier, Ms. M.P. Gower, Ms. N.M. Kuney, Ms. R.T. Krebs, Ms. S.W. Pearce, Ms. K.D. Vick, Ms. L. McDonald, Ms. A.J. Parham, Mr. M.D. Crews, Mr. C.G. Leach, Ms. A.B. Goodman, and Mr. T.W. Wiley. Bulk chemical analysis and handling, dose formulation, and dose formulation analysis were provided by the sponsor through Dr. E.A. Crecelius, PNNL, Battelle Marine Sciences Laboratory, Sequim, WA. Mr. M.M. Veselica (Supervisor, RTI Materials Handling Facility), Mr. D.L. Hubbard, and Mr. R.A. Price provided receipt and disbursement of dose formulations at RTI. Animal care was provided by Dr. D.B. Feldman, DVM, ACLAM, RTI Veterinarian, and Mr. F.N. Ali, Manager of RTI Animal Research Facility. Histology support was provided by EPL, Inc., and Dr. J.C. Seely (EPL) provided pathology support. RTI Quality Assurance personnel were Ms. D.A. Drissel, Ms. D.J. Smith, Ms. M.D. Phillips, Ms. T.M. Kenney, Ms. C. Ingalls, and Ms. M. Oh. Ms. K.D. Andrews, QA Consultant, audited the hormone data.

The final report was prepared by Dr. J.D. George, with assistance from Dr. R.W. Tyl, Ms. B. Hamby, Ms. C.B. Myers, and Ms. M.C. Marr. Ms. C.B. Myers was responsible for data compilation and statistical analyses, assisted by Mr. T.W. Wiley on data entry. Ms. M.C. Marr was responsible for all activities concerning organization and custody of the study records, and for archiving the study records. Ms. D.B. Bynum and Ms. K. L. Kehagias provided secretarial assistance.

Histopathology Report, Analytical Report, Feed Analysis Report, Protocol, Protocol Amendments, and Protocol Deviations

The histopathology and bulk chemical and dose formulation analytical reports were prepared and signed by their respective author(s) and included as Appendix II and III of this report, respectively. The feed analysis reports were produced by PMI, Inc., and included as Appendix IV. The protocol and two amendments, detailing the design and conduct of the study are presented in Appendix V of this report. Protocol deviations are listed on page 36 following the references.

Storage of Records

All original data sheets and records collected during the present study will be stored in the RTI Archives, under the control of the RTI Health Sciences Archivist, and remain the responsibility of RTI. Worksheets and computer printouts, which were generated in the statistical analysis of data, are stored in the RTI Archives. Copies of this report are filed with the RTI Archives and with Battelle. All remaining dose formulations were shipped back to the Sponsor. Records and samples from this study in RTI Archives may be released to the Sponsor upon written request.

Compliance

All records, data, biological specimens, and reports will be maintained in storage for the time period specified by the contract or for as long as the quality of the preparation affords evaluation, whichever is less. Quality control (QC) and quality assurance (QA) procedures followed those outlined in the Quality Assurance Project Plan (QAPP) prepared for this study and in accordance with the Quality Management Plan (QMP) for this project. The RTI Animal Research Facility is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AAALAC), International. At all times, animals were housed, handled, and used according to the NRC Guide (NRC, 1996).

RESULTS

Dose Formulations

Analysis of dose formulations prior to shipping from Battelle-Sequim, to RTI International indicated that the formulations were 91-109.6% of the target concentrations and were homogeneous (Table 1-A to 1-H). Aliquots of the dosing solutions and the control formulations were scheduled to be taken the first day of dosing (the first pnd 23) and on the first pnd 30, 37, 44, and 51. For Component 1, pnd 23, 30, 37, and 44 corresponded to October 7, 14, 21, 28, 2002. For the pnd 51 sample, the dosing formulation remaining in the dosing jar after completion of dosing served as the analytical sample (jar samples), since there was not enough formulation left over to take a separate analytical sample. For Component 2, pnd 23, 30, 37, 44 and 51 corresponded to January 26, 2003 and February 2, 9, 16, and 23, 2003, respectively. In addition, the formulation remaining in the dosing jar was submitted for analysis

(designated as Remain, Remainder, or Rec. samples; see Tables 1-A to 1-H and chemistry reports in Appendix III).

Analysis of 15 mg/ml atrazine dose formulations indicated concentrations of 112 -114% of the target concentration for the in-life samples and 94% of the target concentration for the postdosing sample (Table 1-A). The 30 mg/ml atrazine formulation assayed at 105-113% for the in-life samples and 96% for the postdosing sample. Analysis of 10 mg/ml p, p'-DDE dose formulations indicated concentrations of 93% of the target concentration for the in-life samples and 94% of the target concentration for the postdosing sample (Table 1-B). The 20 mg/ml p, p'-DDE formulation assayed at 91-92% for the in-life samples and 102% for the postdosing sample. The vinclozolin formulations were consumed during dosing, so there was none available to take in-life samples. Analysis of 6 mg/ml vinclozolin dose formulations indicated 95.3% of the target concentration for the postdosing sample (Table 1-C). The 20 mg/ml vinclozolin formulation assayed at 90% for the postdosing sample. Analysis of 5 mg/ml methoxychlor dose formulations indicated concentrations of 90-109% of the target concentration for the in-life samples and 91-94% of the target concentration for the postdosing samples (Table 1-D). The 10 mg/ml methoxychlor formulation assayed at 91-99% for the in-life samples and 91-94% for the postdosing samples.

Analysis of 0.4 mg/ml propylthiouracil dose formulations indicated concentrations of 75-88% of the target concentration for the in-life samples and 124% of the target concentration for the postdosing sample (Table 1-E). The 5 mg/ml propylthiouracil formulation assayed at 83-108% for the in-life samples and 104% for the postdosing sample. These results suggest that the 0.4 mg/ml dosing solution was more difficult to keep homogeneous during the dosing period. Analysis of 10 mg/ml ketoconazole dose formulations indicated concentrations of 85-102% of the target concentration for the in-life samples and 101% of the target concentration for the postdosing sample (Table 1-F). The 20 mg/ml ketoconazole formulation assayed at 91-99% for the in-life samples, and100% for the postdosing sample. Analysis of 10 mg/ml linuron dose formulations indicated concentrations of 99-123% of the target concentration for the in-life samples, and 119% of the target concentration for the postdosing sample (Table 1-G). The 20 mg/ml linuron formulation assayed at 95-106% for the in-life samples, and 97% for the postdosing sample. Analysis of 10 mg/ml phenobarbital dose formulations indicated concentrations of 94-103% of the target concentration for the in-life samples, and 100% of the target concentration for the postdosing sample (Table 1-H). The 20 mg/ml phenobarbital formulation assayed at 99-103% for the in-life samples, and 101% for the postdosing sample. Additional analytical data are presented in Appendix III.

Component 1

Control F1 Males

Fifteen untreated F1 males were assigned to the control group for Component 1. These animals served as the concurrent control group for the animals in Component 1 that were treated with atrazine,

p,p'-DDE, vinclozolin, and methoxychlor. Twelve control animals were evaluated at scheduled necropsy on pnd 52 or 53 (see below).

In-Life Data from F1 Males Treated with Atrazine

Fifteen untreated F1 males were assigned to the 0, 75, or 150 mg/kg/day atrazine group (Table 2-A). No animals assigned to the control group or the high-dose atrazine-treated groups died prior to scheduled necropsy. Three males in each of the control and high dose groups were removed from the study because their correct postnatal day 0 could not be determined. One male in the low-dose group was removed from the study because it was not dosed on the correct postnatal days, and another male was removed from this group because his postnatal day 0 could not be determined. In addition, one male in the low-dose group was found dead on pnd 37 (misdirected dose) and was removed from subsequent evaluation in the study. Thus, there were 12 males in each of the 0, 75, and 150 mg atrazine/kg/day groups that reached scheduled sacrifice. Body weight at weaning (pnd 21), prior to dosing (pnd 22), and on the day of initiation of dosing (pnd 23) was equivalent across treatment groups (Table 3-A). Daily body weights for F1 males were significantly decreased in the high-dose group compared to the control group from pnd 24 to scheduled necropsy on pnd 52 or 53. In the low-dose group, body weight was decreased compared to the control group beginning on pnd 31, and continuing until necropsy. Body weight change was equivalent across treatment groups for pnd 21 to 23, but was significantly less in the low- and high-dose atrazine-treated groups compared to the control group for all intervals from pnd 23 to necropsy on pnd 52 or 53 (Table 3-A).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) was greater in both the low- and high-dose atrazine-treated groups compared to the control group (51% and 39% increase, respectively; Table 4-A). The low- and high-dose atrazine-treated groups exhibited a significant decrease in absolute feed consumption (34.0-28.0% and 27.0-42.1%, respectively) on pnd 22 to 23 and 23 to 24, which was most likely influenced by aversion to taste after the initiation of gavage dosing with the test compound (for pnd 23 to 24). Thereafter, the high-dose group exhibited an effect on absolute feed consumption, with decreases (range of 11.3% to 27.9%) for pnd 24 to 25, 25 to 26, 26 to 27, 27 to 28, 29 to 30, 32 to 33, 33 to 34, 36 to 37, 37 to 38, 43 to 44, 44 to 45, 45 to 46, 46 to 47, 48 to 49, 49 to 50, and 50 to 51. The low-dose group exhibited a significant decrease in absolute feed consumption for pnd 26 to 27, 36 to 37, 43 to 44, 50 to 51, and 52 to 53. Absolute feed consumption for the treatment period (pnd 23 to 52) was significantly decreased at the high dose (by 7.9%). When feed consumption was calculated as a percent of body weight (g/kg/day), the effects of atrazine treatment were not as consistent. Prior to initiation of dosing, relative feed consumption exhibited an increasing trend with both the low and high dose group significantly increased compared to the control on pnd 21 to 22, and a decreasing trend, with both treatment groups significantly decreased compared to the control group on pnd 22 to 23 (reduced by 33.9 and 29.2%, low- and high-dose groups, respectively). Relative feed consumption exhibited a dose-related decrease for pnd 23 to 24, with both atrazine-treated groups affected (reduced by 25.7% and 38.6% at the low- and high-dose, respectively). Relative feed consumption was also decreased

at the high dose for pnd 24 to 25, and 26 to 27. Thereafter, relative feed consumption tended to level out across the treatment groups, with a significant increase in relative feed consumption observed on pnd 28 to 29, 35 to 36, 42 to 43, 47 to 48, and 51 to 52 (both atrazine-treated groups increased), pnd 34 to 35 (low dose only), and pnd 38 to 39 and 39 to 40 (high dose only). A significant decrease in relative feed consumption (ANOVA, $p<0.05$, Linear Trend $p>0.05$) was noted at the low dose only, on pnd 50 to 51. A statistically significant overall treatment effect, but no significant trend or pairwise differences from the control group, was observed on pnd 52 to 53. Relative feed consumption was significantly increased in both atrazine-treated groups when calculated for the whole treatment period ending on pnd 52 (i.e., pnd 23 to 52; by 3.9% and 5.1%, low- and high-dose group, respectively), and for pnd 23 to 53 (by 4.6 and 6.3% low- and high-dose group, respectively; Table 4-A).

Clinical observations were noted in the atrazine-treated groups, and included efflux of the dosing solution, rooting postdosing, rooting prior to dosing, rust-colored fur, salivation postdosing, and salivation prior to dosing in 2, 11, 2, 1, 1, and 12 animal(s) in the high-dose group, respectively (Table 5-A). Efflux of the dosing solution, rooting postdosing, and salivation prior to dosing were observed in four, six, and eight animals, respectively, in the low-dose group. Two control animals exhibited salivation prior to dosing (Table 5-A).

Treatment with atrazine had no significant effect on the average postnatal day of preputial separation (42.0-42.9 days of age; Table 6-A). Average body weight on the day of acquisition was significantly decreased at the high dose (by 8.8% compared to the control group); the low-dose group exhibited a smaller decrease (by 4.9%) which was not statistically significant (Table 6-A).

Necropsy and Histopathological Data from F1 Males Treated with Atrazine

At necropsy, average body weight exhibited a dose-related decreasing trend, with the low- and high-dose atrazine-treated groups significantly below the control group (Table 7-A). Absolute paired kidney and epididymides weights, prostate weight, and LABC muscle weight were decreased at the high dose, whereas pituitary, liver and seminal vesicle with coagulating glands weight were decreased at both doses of atrazine. A significant dose-related decreasing trend was observed for ventral and dorsolateral prostate weight with no significant pairwise differences. When organ weights were adjusted with respect to necropsy body weight, paired testes weight exhibited a dose-related increasing trend. Atrazine treatment had no significant effect on T4 or thyroid stimulating hormone (TSH) levels (Table 7-A).

Gross necropsy findings were minimal, and included one animal each in the control and low-dose group, and two animals in the high-dose group with hydronephrosis, and one animal in the low-dose group with a small, undescended testis and a small left epididymis (Table 8-A). No treatment-related histopathology was observed.

In-Life Data from F1 Males Treated with p, p'-Dichlorodiphenyldichloroethylene

Fifteen untreated F1 males were assigned to the 0, 50, or 100 mg/kg/day p, p'-DDE groups (Table 2-B). Three control animals and one low dose animal were removed from the study because their correct postnatal day 0 could not be determined. One animal in the 50 mg/kg/day group was euthanized on pnd 29 due to a leg injury. Thus, 12, 13, and 15 F1 males were available for evaluation at necropsy. Body weight at weaning (pnd 21), prior to initiation of dosing (pnd 22), and on the day of initiation of dosing (pnd 23) was equivalent across treatment groups (Table 3-B). Body weight and body weight change were not affected by treatment with p,p'-DDE.

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) was equivalent across dose groups, but was reduced at both doses of p, p'-DDE (by 28.0 and 23.0% compared to control) for pnd 22 to 23 (Table 4-B). The high-dose p, p'-DDE-treated group exhibited a significant decrease in absolute feed consumption (by 11.2-12.5%) on pnd 23 to 24 and 26 to 27. Thereafter, the high-dose animals tended to consume more feed (g/day) than the control group. Significantly increased feed consumption in the high-dose group was observed on pnd 28 to 29 (by 17.6%), 41 to 42 (by 12.5%), pnd 42 to 43 (by 13.5%), pnd 47 to 48 (by 17.5%) and pnd 50 to 51 (by 19.3%). Similar significant increases were noted in the low-dose group accompanied by a significant linear trend on pnd 47 to 48 and on 51 to 52 in the absence of a significant linear trend. An increasing trend, only, was noted on pnd 35 to 36, 38 to 39, 39 to 40, and 48 to 49. Absolute feed consumption was significantly increased in the high-dose group for the treatment period measured from pnd 23 to 52 (by 6.9%). When feed consumption was calculated as a percent of body weight (g/kg/day), a significant decrease was noted in the high-dose group compared to the control group for pnd 23 to 24, and 26 to 27 (8.5 and 10.2%, respectively). A significant increase in relative feed consumption was observed in both the low and high groups for pnd 28 to 29, 35 to 36, 38 to 39, 39 to 40, 42 to 43, and 47 to 48. In addition, relative feed consumption was significantly increased at the high dose of p, p'-DDE on pnd 37 to 38, 41 to 42, 48 to 49, 50 to 51, pnd 23 to 52, and pnd 23 to 53. An increasing trend was noted for pnd 49 to 50 and 52 to 53. Non-dose related increases were observed at the low dose for relative feed consumption on pnd 24 to 25, and 51 to 52, and significant overall treatment effects (ANOVA, $p>0.05$) were observed in the absence of a linear trend or pairwise differences from the control group on pnd 31 to 32 and 32 to 33 (Table 4-B).

Clinical observations were noted in the p, p'-DDE-treated groups, and consisted of chromodacryorrhea, efflux of the dosing solution, rooting postdosing, and salivation prior to dosing, in one, one, nine, and three animal(s) in the high-dose group, respectively, and chromodacryorrhea, rooting postdosing, rust-colored fur, and salivation prior to dosing in one each in the low-dose group. Two control animals were observed to salivate prior to dosing (Table 5-B).

Treatment with p, p'-DDE significantly delayed preputial separation in the low- and high-dose groups (44.9 and 45.7 days, respectively) compared to the control group (41.4 days; Table 6-B). On the

day of acquisition, average body weight in the low-dose group was increased by 14.4%, and by 18.1% in the high-dose group, compared to the control group value.

Necropsy and Histopathological Data from F1 Males Treated with p, p'-Dichlorodiphenyldichloroehtylene

At necropsy, average body weight was equivalent across treatment groups (Table 7-B). Absolute weight of the pituitary, paired adrenal glands, paired testes, ventral and dorsolateral prostate, whole prostate, seminal vesicles and coagulating glands, and LABC was unaffected by p, p'-DDE treatment. Absolute thyroid, liver, and paired kidney weight were increased at both doses of p, p'-DDE, whereas paired epididymides weight was decreased at the high dose. When organ weights were adjusted with respect to body weight at necropsy, thyroid, liver, and paired kidney weights were significantly increased at both doses of p, p'-DDE. Adjusted paired epididymides weight was decreased at the high dose, whereas the adjusted weight of the LABC exhibited a decreasing linear trend with no significant pairwise comparisons. T4 levels (in microg/dL) exhibited a decreasing trend, and were significantly decreased at the high dose (by 17.8% compared to the control value). TSH levels (ng/ml) were slightly increased in a dose-related manner (28.4 and 31.7%, compared to the control group values), but these differences did not reach statistical significance. (Table 7-B).

Gross necropsy findings were minimal, and included hydronephrosis in one animal in the control group, one animal in the low-dose group, and four animals in the high-dose group, and one animal each in the high-dose group with chromodacryorrhea or intestines distended with air (Table 8-B). No treatment-related histopathology was observed.

In-Life Data from F1 Males Treated with Vinclozolin

Fifteen untreated F1 males were assigned to the 0, 30, or 100 mg/kg/day vinclozolin groups (Table 2-C). No animals died prior to scheduled necropsy on pnd 52 or 53. Three males in the control and high-dose groups, and two males in the low-dose group were removed from the study because their correct postnatal day 0 could not be confirmed. Thus, 12, 13, and 12 animals were available in the control, low-, and high-dose groups, respectively, for full evaluation in this study. Body weight at weaning (pnd 21), pnd 22, and on the day of initiation of dosing (pnd 23) was equivalent across treatment groups (Table 3-C). In addition, daily body weights for F1 males were unaffected by vinclozolin treatment through pnd 53. Body weight change was equivalent across treatment groups for all intervals except pnd 51 to 53, which exhibited an increase at the low but not the high dose (Table 3-C).

Feed consumption (g/day) was equivalent across treatment groups for all intervals, with the following exceptions. A decreasing trend, only, was noted for pnd 26 to 27, and 45 to 46. On pnd 47 to 48, vinclozolin-treated groups were significantly increased over the control group in the presence of a significant increasing trend, and on pnd 51 to 52 in the absence of a significant trend. A transient decrease was also noted in the low dose for pnd 27 to 28. Absolute feed consumption for the entire treatment period (pnd 23 to pnd 52 or 53) was statistically equivalent across treatment groups. When feed

consumption was calculated as a percent of body weight (g/kg/day), a decreasing trend, only, was noted for pnd 23 to 24, and for pnd 45 to 46. However, relative feed consumption was increased in the high-dose group for pnd 24 to 25 (by 10.6%), 25 to 26 (by 14.0%), 30 to 31 (by 12.5%), 39 to 40 (by 7.6%), and 23 to 53 (by 4.7%), and in both vinclozolin-treated groups on pnd 28 to 29, 47 to 48, and 51 to 52 (by a range of 12.6 to 20.2%). An increasing trend, only, was noted for pnd 31 to 32, 37 to 38, and 42 to 43, but no significant differences between the control group and either of the treated group values were noted. A decreasing trend was observed for pnd 45 to 46. A transient increase in relative feed consumption, in the absence of a significant trend, was observed at the low dose for pnd 35 to 36. Relative feed consumption was equivalent across treatment groups when calculated for pnd 23 to 52 (Table 4-C).

Clinical observations were noted in the vinclozolin-treated groups, and consisted of efflux of dosing solution, piloerection, rooting postdosing, and salivation prior to dosing in three, one, four, and five high-dose animal(s), respectively, and efflux of the dosing solution, rooting postdosing, salivation prior to dosing, and sore(s) in one, four, two, and one low-dose animal(s), respectively (Table 5C). Two animals in the low-dose group were not dosed with vinclozolin on pnd 50, because there was not enough dosing solution. These animals resumed dosing the following day until scheduled necropsy. Two control animals exhibited salivation prior to dosing (Table 5-C).

Treatment with vinclozolin resulted in a dose-related delay in preputial separation that was significant in both treated groups (Table 6-C). The average postnatal day of preputial separation was 43.8 and 46.8 for the low- and high-dose groups, respectively, compared to 41.4 days for the control group. Body weight on the day of acquisition of preputial separation was significantly increased for both the low and the high dose vinclozolin-treated groups, likely secondary to the older age of these animals. Two males in the high-dose group failed to acquire preputial separation by pnd 52, and were therefore excluded from the calculation of this parameter. It is not known whether these animals would have exhibited preputial separation if the study had been extended (Table 6-C).

Necropsy and Histopathological Data from F1 Males Treated with Vinclozolin

At necropsy, average body weight exhibited a decreasing trend that was not dose-related (Table 7-C). Absolute pituitary, thyroid, liver, paired adrenal, paired kidney and paired testes weights were unaffected by treatment with vinclozolin. However, absolute paired epididymides, dorsolateral prostate, whole prostate, seminal vesicles with coagulating glands, and LABC weights were decreased at the high dose. Ventral prostate weight exhibited a decreasing trend. When organ weights were adjusted with respect to necropsy body weight, paired testis weight was increased at both doses of vinclozolin. Adjusted paired epididymides, and seminal vesicles with coagulating gland weights were decreased at both dose levels. Adjusted dorsolateral prostate, total prostate, and LABC weights were decreased at the high dose, and ventral prostate weight exhibited a decreasing trend. Vinclozolin treatment had no significant effect on adjusted pituitary, thyroid, liver, paired adrenal, or paired kidney weight. T4 was significantly decreased at both doses of vinclozolin, whereas TSH levels were unaffected (Table 7-C).

Gross necropsy findings were minimal, and included one to four animals in each group with hydronephrosis, and one animal in the high-dose group that had small seminal vesicles (Table 8-C). No treatment-related histopathology was observed.

In-Life Data from F1 Males Treated with Methoxychlor

Fifteen untreated F1 males were assigned to the 0, 25, or 50 mg/kg/day methoxychlor groups (Table 2-D). No animals died from the study prior to scheduled necropsy on pnd 52 or 53. Three animals in the control group and two animals in the high-dose group were removed from the study because their correct postnatal day 0 could not be determined. Thus, 12, 15, and 13 animals were available for full evaluation in the control-, low-, and high-dose groups, respectively, in this study. Body weights at weaning (pnd 21), pnd 22, and on the day of initiation of dosing (pnd 23) were equivalent across treatment groups (Table 3-D). In addition, daily body weights for F1 males were unaffected by methoxychlor treatment through pnd 53. Body weight change was equivalent across treatment groups for pnd 21 to 23, 23 to 30, 30 to 37, 51 to 52, 51 to 53, and 23 to 53. A decreasing trend was noted for pnd 37 to 44, 44 to 51, and for pnd 23 to 52. The high-dose group gained significantly less weight than the control group for the periods of pnd 37 to 44 and 44 to 51 (Table 3-D).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of dosing) was increased in animals assigned to the high dose groups (Table 4-D). For pnd 22 to 23, feed consumption exhibited a decreasing trend. After initiation of dosing, an increasing trend was noted for absolute feed consumption on pnd 25 to 26, but no other effects of treatment on feed consumption were noted until pnd 43 to 44. Absolute feed consumption on pnd 43 to 44 exhibited a decreasing trend, with the high-dose significantly reduced (by 13%) compared to the control group. A transient decrease in absolute feed consumption, in the absence of a significant trend, was noted for the low dose group on pnd 45 to 46. On pnd 47 to 48, an increasing trend was noted with the high dose group significantly increased (by 13.2%) compared to the control group. A decreasing trend was also noted for pnd 51 to 52. Absolute feed consumption for the entire treatment period (pnd 23 to pnd 52 or 53) was statistically equivalent across treatment groups. When feed consumption was calculated as a percent of body weight (g/kg/day), a significant increase was noted for animals assigned to the high-dose group on pnd 21 to 22, prior to initiation of dosing. On pnd 22 to 23, the high-dose group exhibited a significant decrease (by 25.5%) compared to the control group. A decreasing trend was noted on pnd 43 to 44. Increases in relative feed consumption were noted at the high dose on pnd 25 to 26, 28 to 29, and 47 to 48 (by 10.9-16.3%), and in the low-dose group on pnd 28 to 29 and 47 to 48 (by 9.9 to 12.7%). Relative feed consumption was equivalent across treatment groups when calculated for the whole treatment period (pnd 23 to 52 or 23 to 53; Table 4-D).

Clinical observations were noted in the methoxychlor-treated groups and consisted of chromodacryorrhea in one animal at the low dose, efflux of dosing solution in two animals at the low dose and one animal at the high dose, and rooting postdosing in two animals at the high dose (Table 5-D). Two control animals exhibited salivation prior to dosing (Table 5-D).

Treatment with methoxychlor had no significant effect on the average day of preputial separation (Table 6-D). The average postnatal day of preputial separation was 41.4, 41.8 and 41.8 for the control, low- and high-dose groups, respectively. Body weight on the day of acquisition of preputial separation was equivalent across the treatment groups (Table 6-D).

Necropsy and Histopathological Data from F1 Males Treated with Methoxychlor

At necropsy, average body weight was equivalent across dose groups (Table 7-D). Absolute pituitary, liver, paired kidney, paired testes, paired epididymides, prostate (ventral, dorsolateral, and total), and LABC weights were not significantly affected by treatment with methoxychlor. Absolute thyroid weight exhibited a significant overall treatment effect (ANOVA, $p<0.05$). A dose-related increasing trend and significant increase at the high dose were observed for absolute paired adrenal weight. Absolute seminal vesicles with coagulating glands weight exhibited a dose-related decreasing trend, with a significant decrease at the high dose of methoxychlor. When organ weights were adjusted with respect to necropsy body weight, paired adrenal gland weight was significantly increased at the high dose and seminal vesicles and coagulating glands weight was decreased at the high dose. T4 and TSH levels were unaffected by treatment with methoxychlor (Table 7-D).

Gross necropsy findings were minimal, and included one animal each in the control and high-dose group with hydronephrosis (Table 8-D). No treatment-related histopathology was observed.

Component 2

Control F1 Males

Fifteen untreated F1 males were assigned to the control group for Component 2. These animals served as the concurrent control group for the animals in Component 2 that were treated with propylthiouracil, ketoconazole, linuron, and phenobarbital. One animal in the control group was found dead on pnd 31 due to a misdirected dose, and was removed from further evaluation in the study.

In-Life Data from F1 Males Treated with Propylthiouracil

Fifteen untreated F1 males were assigned to the 0, 2, or 25 mg/kg/day propylthiouracil groups (Table 2-E). One animal in the control group was found dead on pnd 31 due to a misdirected dose, and was removed from the study, and one animal in the high-dose group was found dead on pnd 50. Thus, 14, 15, and 14 animals were available for full evaluation in the control, low, and high-dose groups in this study. Body weight at weaning (pnd 21), pnd 22, and on the day of initiation of dosing (pnd 23) was equivalent across treatment groups (Table 3-E). In addition, daily body weights for F1 males were unaffected by propylthiouracil treatment through pnd 31. A significant dose-related decreasing trend was observed for all time points from pnd 32 through necropsy on pnd 52 or 53, with the high-dose group significantly decreased compared to the control group at all time points beginning with pnd 33. The reductions in body weight at the high dose were progressive with dosing, and reached 45.0-46.3% of the

control value by pnd 52-53. The low-dose group did not exhibit any significant reduction in body weight until necropsy, and was reduced then only by 7.6-9.5% compared to the control values. Body weight change was equivalent across treatment groups for pnd 21 to 23, and pnd 23 to 30. Beginning on pnd 30 to 37, a decreasing trend was noted that continued through necropsy on pnd 52 or 53. The high-dose group gained significantly less weight than the control group for all periods beginning on pnd 30. Weight gain in the high-dose group slowed progressively, from 41.7% less than the controls for pnd 30 to 37 to no or almost no measurable weight gain on pnd for pnd 51 to 52 and 51 to 53. Weight gain in the low-dose group was significantly and progressively reduced compared to the control group beginning on pnd 44, although less affected than the high-dose group (29.5 to 66.3% less than the controls). Overall weight change during the treatment period until necropsy on pnd 52 or 53 was significantly reduced in both the low (by 9.6-12.7%) and high (by 56.8-58.1%) dose groups, compared to the control group value (Table 3-E).

Feed consumption (g/day) for pnd 21 to 22 and pnd 22 to 23 (prior to initiation of dosing) was equivalent across treatment groups (Table 4-E). After initiation of dosing on pnd 23, absolute feed consumption continued to be unaffected by treatment until pnd 30, with the exception of a transient increase at the low dose for pnd 25 to 26. Thereafter, a decreasing trend was noted for feed consumption for every interval, beginning on pnd 30 until necropsy on pnd 52 or 53. The high-dose group ate significantly and progressively less feed (g/day) than the control group, beginning on pnd 31 (16.6 to 62.5% less than the control group value). The low-dose group exhibited this same effect, although less severe, beginning on pnd 45 (9.2 to 29.0% reduction in feed consumption). Absolute feed consumption for the entire treatment period (pnd 23 to pnd 52 or 53) was reduced at the high dose (by 35.3-38.5%) dose compared to the control group value. When feed consumption was calculated as a percent of body weight (g/kg/day), a similar pattern was observed. Reductions in feed consumption in the high-dose group were observed beginning on pnd 31, ranged from 6.4% to 33.8% and generally increased with extended dosing. Beginning on pnd 44, the low-dose group exhibited reduced feed consumption that ranged from 7.6% to 21.9% less than the control group. Relative feed consumption for the whole treatment period (pnd 23 to 52 or 23 to 53) was reduced by 14.1-16.5% in the high-dose group. The low-dose group exhibited reduced relative feed consumption only for the treatment period ending on pnd 52 (by 3.4%) but not for pnd 23 to 53 (Table 4-E).

Clinical observations were noted in the propylthiouracil-treated groups, and consisted of efflux of the dosing solution, rooting postdosing, rough coat, and salivation prior to dosing in 1, 2, 1, and 1 animal(s) in the low-dose group, and efflux of the dosing solution, rooting postdosing, and salivation prior to dosing in 1, 14, and 1 animal(s) in the high-dose group (Table 5-E). The control animals had no distinctive clinical signs (Table 5-E).

Treatment with propylthiouracil significantly delayed acquisition of preputial separation in the high-dose group (Table 6-E). The average postnatal day of preputial separation was 40.4 and 43.3 for the

low- and high-dose groups, respectively, compared to 39.6 days for the control group. Body weight on the day of acquisition of preputial separation was significantly decreased at the high dose.

Necropsy and Histopathological Data from F1 Males Treated with Propylthiouracil

At necropsy, average body weight exhibited a decreasing trend that was dose-related (Table 7-E). The high-dose animals exhibited a dose-related increase in absolute thyroid weight, with both propylthiouracil-treated groups significantly increased over the control group value. All other organ weights exhibited a dose-related decreasing trend, with all absolute organ weights except seminal vesical weight significantly reduced at the high dose. Low dose animals had reduced absolute liver, paired adrenal gland, and paired kidney weight. When organ weights were adjusted with respect to necropsy body weight, both the thyroid and the seminal vesicles with coagulating glands exhibited increased adjusted organ weight for both treatment groups. The adjusted weights of the paired adrenal glands and the paired kidneys were significantly decreased at the low dose, although there was not a statistically significant change at the high dose. Adjusted paired epididymides weight exhibited an increasing trend. T4 levels were significantly reduced at both dose levels, in a dose-related manner, and TSH levels were significantly increased in a dose-related manner at both doses (Table 7-E).

Gross necropsy findings included one animal in the control group with urinary calculi and thickened bladder wall, one animal each in the low-dose group exhibiting hydronephrosis, pulmonary foci, reduced dorsolateral or ventral prostate, or reduced seminal vesicles, and nine animals with enlarged and/or otherwise notable thyroid glands (Table 8-E). In the high-dose group, 4 animals had reduced adrenal glands, 2 animals had hydronephrosis, 1 animal had small kidneys, pituitary, dorsolateral prostate, or ventral prostate, 6 animals had hepatic abnormalities (mottled or reduced in size), and 14 animals had thyroid observations , including enlargement, reddening, or darkening (Table 8-E). All animals in the high-dose group exhibited thyroid follicular cell hypertrophy/hyperplasia, characterized by increased size and apparent number of follicular cells, and reduction of follicular lumen size. The severity of these changes were scored as:

- minimal = multifocal follicles affected, with size and number of follicular cells slightly enlarged and increased;
- mild = diffuse change with further increased cell size and hyperplasia;
- moderate = enhanced severity with the presence of notable numbers of follicular cell mitoses; and
- marked = increased mitotic rate, some degenerative cells within the follicular epithelium, and obvious enlargement of the thyroid shape and size.

Based on these criteria, no animals were scored as minimal, one animal was scored as mild, nine moderate, and four marked at the high dose. Based on these results, the low dose thyroids were also examined, revealing that all 15 animals at the low dose also exhibited thryoid hypertrophy/hyperplasia. As would be expected, the severity was somewhat less, with scores of 0 minimal, 10 mild, 5 moderate,

and no markedly affected animals. These changes were reflected in the dose-related increases in adjusted thyroid weight (for body weight at necropsy) at both dose levels.

In-Life Data from F1 Males Treated with Ketoconazole

Fifteen untreated F1 males were assigned to the 0, 50, or 100 mg/kg/day ketoconazole group (Table 2-F). One animal each in the control and high-dose group died of a misdirected dose on pnd 31 and 37, respectively, and was removed from further evaluation in the study. Thus, 14, 15, and 14 F1 males were available for evaluation at scheduled necropsy. Daily body weight and body weight change from pnd 23 to pnd 52 or 53 were largely unaffected by treatment with ketoconazole (Table 3-F). A significant decreasing trend was observed for body weight on pnd 46, 48, and 49, and for body weight change on pnd 44 to 51 and 23 to 52 but with no pairwise difference from controls. No other changes were noted (Table 3-F).

Absolute feed consumption on pnd 21 was increased in animals assigned to the low and the high-dose groups (Table 4-F). Thereafter, absolute feed consumption for intervals between pnd 23 and pnd 52 or 53 was equivalent across the groups, with the exception of transient increases at the low dose on pnd 23 to 24, and 36 to 37. Absolute feed consumption for pnd 23 to 52 was equivalent across the treatment groups; an increasing trend was noted for pnd 23 to 53. When feed consumption was calculated as a percent of body weight (g/kg/day), feed consumption exhibited an increasing trend and significant increases for animals assigned to either the low- or the high-dose group on pnd 21 to 22. For pnd 23 to 24 (after initiation of treatment), relative feed consumption was also increased in both the low- and high-dose groups. Increased relative feed consumption was noted in the high-dose group on pnd 41 to 42, 43 to 44, and 49 to 50 (10.4, 10.7, and 8.5%, respectively). A transient increase in relative feed consumption was noted in the low dose group on pnd 36 to 37. A dose-related increasing trend, only, was noted for pnd 46 to 47 and pnd 50 to 51. Relative feed consumption for the treatment period of pnd 23 to 52 or pnd 23 to 53 was increased in both the low (by 3.7 to 6.2%) and the high (by 4.7 to 7.6%) dose groups compared to the control group values (Table 4-F).

Clinical observations noted in the ketoconazole-treated groups consisted of efflux of dosing solution, rooting postdosing, rooting prior to dosing, rough coat, and salivation prior to dosing in 1, 14, 1, 1, and 4 animal(s) in the low-dose group, respectively, and efflux of dosing solution, piloerection, rooting postdosing, rough coat, and salivation prior to dosing in 1, 1, 15, 2, and 13 animal(s) in the high-dose group, respectively (Table 5-F).

Treatment with ketoconazole resulted in a significant delay in the average postnatal day of preputial separation at both treatment levels (Table 6-F). Acquisition of preputial separation occurred at 42.3 days in the low-dose group and 44.1 days in the high-dose group, compared to 39.6 days for the control group. Body weight on the day of acquisition was increased in a dose-related manner, likely reflecting the older age of the ketoconazole-treated animals.

Necropsy and Histopathological Data from F1 Males Treated with Ketoconazole

At necropsy, average body weight was equivalent across treatment groups (Table 7-F). Absolute paired adrenal weights were increased in a dose-related manner at both treatment levels of ketoconazole. Paired testes, paired epididymides, ventral prostate, total prostate, and LABC weight exhibited dose-related decreasing trends. Seminal vesicles with coagulating glands weight was significantly decreased at both treatment levels, whereas, testes weight was decreased at the high dose. When organ weights were adjusted with respect to necropsy body weight, liver weight and paired adrenal glands weight were significantly increased at both treatment levels, whereas seminal vesicles with coagulating glands weight was decreased at both treatment levels. Adjusted paired kidney weight increased in a dose-related manner that was significant at the high dose of ketoconazole, whereas adjusted paired testes weight was significantly decreased at the high dose. Ketoconazole treatment had no significant effect on T4 or TSH levels (Table 7-F).

Gross necropsy findings included abnormal adrenal gland, hydronephrosis, small dorsolateral prostate, and small seminal vesicles in four, one, one, and one animal(s) in the low-dose group, respectively, and abnormal adrenal gland, hydronephrosis, pulmonary foci, small dorsolateral prostate, small ventral prostate, and small seminal vesicles in six, two, one, one, three, and four animal(s) in the high-dose group (Table 8-F). One control animal had urinary calculi and thickened bladder wall (Table 8-F). No treatment-related histopathology was observed.

In-Life Data from F1 Males Treated with Linuron

Fifteen untreated F1 males were assigned to the 0, 50, or 100 mg/kg/day linuron group (Table 2-G). One animal assigned to the control group was found dead on pnd 31 due to a misdirected gavage dose, and was removed from further evaluation in the study. Thus, there were 14, 15, and 15 F1 males available for evaluation in the control, low- and high-dose groups, respectively, at scheduled necropsy. Body weights were equivalent across treatment groups from pnd 21 to pnd 23 (Table 3-G). Thereafter, a significant decreasing trend was observed for daily body weights until scheduled necropsy on pnd 52 or 53. The high-dose group weighed significantly less than the control group every day from pnd 25 to pnd 52. Daily body weight in the low-dose group was significantly less than the control group during the middle portion of the dosing period, i.e., pnd 32 to pnd 43, with the exception of pnd 36. Body weight change exhibited a decreasing trend for all interim time intervals between pnd 21 and pnd 52, with the high dose significantly decreased for each interim interval from pnd 23 to pnd 52. Body weight change was significantly reduced at the low dose for pnd 23 to 30, and 30 to 37. Body weight change for pnd 51 to 53 was equivalent across treatment groups. However, body weight change for the entire treatment period from pnd 23 to pnd 52 was significantly reduced at both dose levels of linuron, whereas body weight change for pnd 23 to 53 was significantly decreased only at the high dose (Table 3-G).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) was increased at the high dose, whereas feed consumption for pnd 22 to 23 was equivalent across treatment groups

(Table 4-G). Absolute feed consumption (g/day) exhibited a decreasing trend for all interim time intervals from pnd 23 to pnd 52, with the exception of pnd 34 to 35, 35 to 36, 37 to 38, 38 to 39, 41 to 42, and 52 to 53, for which feed consumption was equivalent across the treatment groups. With the exception of pnd 27 to 28, and 42 to 43, the high-dose animals consumed significantly less feed than the control animals at each of these intervals (by 8.4 to 21.1% less than the control group). The low-dose group consumed 6.8 to 14.9% less feed than the control animals for a brief period (pnd 23 to 24, 24 to 25, 25 to 26, 28 to 29, and 31 to 32). With regard to the whole treatment period for animals necropsied on pnd 52, the high-dose animals consumed 13.7% less feed than the control animals. Feed consumption for the whole treatment period from pnd 23 to 53 exhibited a decreasing trend, but with no significant differences from the control group for either the low- or high-dose group. When feed consumption was calculated as a percent of body weight (g/kg/day), feed consumption was more consistent across treatment groups. Relative feed consumption was increased in animals assigned to the high dose on pnd 21 to 22 (prior to the start of dosing). On pnd 24 to 25, 25 to 26, and 26 to 27, relative feed consumption exhibited a decreasing trend, with the high-dose animals consuming 10.4 to 11.0% less than the control animals on pnd 24 to 25, and 25 to 26, and the low dose animals consuming 10.5% less than the control animals on pnd 24 to 25. Thereafter, relative feed consumption was equivalent across treatment groups, with the exception of a decrease in both treatment groups on pnd 31 to 32 (7.0%, low; 10.7%, high), an increasing trend on pnd 46 to 47 and 47 to 48, and significantly increased relative feed consumption in the low (8.0%) and high (6.0%) dose groups, compared to the control group on pnd 47 to 48. On pnd 43 to 44, relative feed consumption in the low-dose group, but not the high-dose group, was transiently increased (8.7%) over the control group value. Relative feed consumption for the entire treatment period (pnd 23 to pnd 52 or 53) was equivalent across treatment groups (Table 4-G).

Clinical observations were noted in the linuron-treated groups, and consisted of rooting postdosing, salivation postdosing, and salivation prior to dosing in 15, 1, and 6 animal(s) in the low-dose group, and difficult (resisting) to dose, efflux of dosing solution, rooting postdosing, and salivation prior to dosing in 1, 1, 15, and 14 animal(s) at the high dose (Table 5-G).

Treatment with linuron significantly delayed preputial separation at both dose levels (Table 6-G). Preputial separation occurred at 43.6 days and 45.5 days in the low- and high-dose groups, respectively, compared to 39.6 days for the control animals. Average body weight at acquisition was significantly increased in both linuron-treated groups, likely reflecting the older age of these animals.

Necropsy and Histopathological Data from F1 Males Treated with Linuron

At necropsy, average body weight exhibited a dose-related decreasing trend, with the low- and high-dose linuron-treated group values significantly below the control group value (Table 7-G). Absolute pituitary, paired kidney, ventral, dorsolateral, and whole prostate, seminal vesicles with coagulating glands and LABC weights decreased in a dose-related manner, with significant reductions at both doses of linuron. Thyroid, liver, paired testes, and paired epididymides weights were decreased only at the high dose. Paired adrenal gland weight was not affected by linuron treatment. When organ weights were

adjusted with respect to necropsy body weight, adjusted liver weight exhibited a significant dose-related increase at both the low- and high-dose of linuron. Adjusted prostate and ventral prostate weight were decreased at the low, but not the high-dose of linuron, whereas adjusted seminal vesicles with coagulating glands weight was decreased at the high dose. T4 levels decreased in a dose-related manner with the values in both linuron-treated groups significantly decreased compared to control values (by 20.4% and 41.2%, low- and high-dose, respectively). TSH levels were significantly decreased at the low dose (by 22.2%) compared to the control animals. The high-dose animals exhibited a 17.8% decrease in TSH levels, but this did not reach statistical significance (Table 7-G).

Gross necropsy findings included two, two, and three animal(s) in the low-dose group with small dorsolateral prostate, small ventral prostate, and small seminal vesicles, respectively, one, one, one, three, four, six, and one animal(s) in the high-dose group with hydronephrosis, reddened lungs, small pituitary, small dorsolateral prostate, small ventral prostate, small seminal vesicles, and enlarged spleen with white foci, respectively. One animal in the control group had urinary calculi and a thickened bladder wall (Table 8-G). No treatment-related histopathology was observed.

In-Life Data from F1 Males Treated with Phenobarbital

Fifteen untreated F1 males were assigned to the 0, 50, or 100 mg/kg/day phenobarbital group (Table 2-H). One animal assigned to the control group was found dead on pnd 31 due to a misdirected gavage dose, and was removed from further evaluation in the study. Thus, there were 14, 15, and 15 F1 males available for evaluation in the control, low- and high-dose groups, respectively at scheduled necropsy. Body weights were generally equivalent across treatment groups from pnd 21 to pnd 53, with the exception of decreasing trends on pnd 32, 33, 34, 37, 38, 39, 49, 50, and 52 with no significant pairwise comparisons (Table 3-H). Body weight change exhibited a decreasing trend for pnd 23 to 30, 30 to 37, and 44 to 51 with the high-dose significantly decreased compared to the control group for pnd 30 to 37. Body weight change for the entire treatment period from pnd 23 to pnd 52 exhibited a decreasing trend with no significant pairwise comparisons, whereas body weight change for pnd 23 to 53 exhibited no statistically significantly changes (Table 3-H).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) was increased in animals assigned to the phenobarbital groups, compared to the animals assigned to the control group, whereas feed consumption for pnd 22 to 23 was equivalent across treatment groups (Table 4-H). Absolute feed consumption (g/day) exhibited increasing trends and significant increases at the high dose compared to the control group values for pnd 25 to 26 and 26 to 27. The low-dose group exhibited a transient increase in feed consumption for pnd 23 to 24. Absolute feed consumption for the whole treatment period, for animals necropsied on pnd 52 or 53, was equivalent across treatment groups. When feed consumption was calculated as a percent of body weight (g/kg/day) the animals assigned to the phenobarbital-treated groups still exhibited significantly increased feed consumption. Increasing trends were noted for pnd 21 to 22, 25 to 26, 26 to 27, 29 to 30, 30 to 31, 36 to 37, 41 to 42, 43 to 44, 44 to 45, 45 to 46, 46 to 47, 47 to 48, 48 to 49, 49 to 50, and 50 to 51. A significant increase in relative feed

consumption was observed in both the low (by 5.4 to 8.5%) and high-dose (by 9.5 to 11.7%) groups on pnd 25 to 26, 26 to 27, 41 to 42, and 43 to 44. Relative feed consumption was significantly increased at the high dose, only (by 8.4 to 14.3%) on pnd 29 to 30, 30 to 31, 46 to 47, and 49 to 50. On pnd 23 to 24, relative feed consumption was transiently increased at the low dose of phenobarbital (by 16.4%) compared to the control group. Relative feed consumption for the entire treatment period (pnd 23 to pnd 52 or 53) was significantly increased in both the low (by 3.8 to 6.8%) and high (by 7.1 to 8.4%) dose phenobarbital-treated groups compared to the control group (Table 4-H).

Clinical observations were noted in the phenobarbital-treated groups, and consisted of ataxia postdosing, efflux of the dosing solution, prone postdosing, rooting postdosing, rough coat, and salivation prior to dosing in 6, 1, 4, 12, 4, and 4 animal(s) in the low-dose group, and ataxia postdosing, efflux of the dosing solution, prone postdosing, rooting postponing, rough coat, and salivation prior to dosing in 5, 1, 15, 15, 3, and 6 animal(s) at the high dose (Table 5-H).

Treatment with phenobarbital significantly delayed preputial separation at both dose levels (Table 6-H). Preputial separation was observed at 41.3 days and 43.0 days in the low- and high-dose groups, respectively, compared to 39.6 days for the control animals. Average body weight at acquisition was significantly increased in the high-dose group, and also increased (biologically significant) at the low dose of phenobarbital, compared to the control group, likely reflecting the older age of these animals.

Necropsy and Histopathological Data from F1 Males Treated with Phenobarbital

At necropsy, average body weight exhibited a dose-related decreasing trend with no significant pairwise comparisons (Table 7-H). Absolute thyroid and liver weight increased in a dose-related manner that was significant at both doses of phenobarbital. Absolute paired testes, paired epididymides, seminal vesicles with coagulating glands, and LABC weight each exhibited a decreasing trend and a significant decrease at the high dose compared to the control group value. When organ weights were adjusted with respect to necropsy body weight, the effects on the thyroid, liver, paired testes, and LABC were the same as observed for the absolute organ weights; paired epididymides weight exhibited a decreasing trend, only. T4 and TSH levels were not affected by phenobarbital treatment (Table 7-H).

Gross necropsy findings included two, one, one, and one animal(s) in the low-dose group with hydronephrosis, small dorsolateral prostate, small ventral prostate, and small seminal vesicles, respectively, two, two, two, and three animal(s) in the high-dose group with hydronephrosis, small dorsolateral prostate, small ventral prostate, and small seminal vesicles, respectively. One animal in the control group had urinary calculi and a thickened bladder wall (Table 8-H). No treatment-related histopathology was observed.

DISCUSSION AND CONCLUSIONS

This study was designed to gather information describing the conduct and usefulness of the male pubertal assay, that has been designated as an optional Endocrine Disruptor Tier I screening protocol (EDSTAC, 1998), using compounds selected to aid in the optimization of the protocol. Currently in the prevalidation stage, the male pubertal assay provides a means of screening apical effects of endocrine disruptors that may alter a number of endocrine-dependent mechanisms, including estrogenic-, androgenic-, and thyroid hormone-related processes (Stoker et al., 2000). As summarized in Stoker et al. (2000), the male pubertal protocol should be able to detect alterations in sexual maturation and thyroid function. The endpoints in the current version of this protocol were chosen to reflect specific changes in pubertal development, thyroid function, or general toxicity. In an effort to evaluate the ability of this protocol to detect alterations in each of these areas, the following compounds were tested: atrazine (affects the hypothalamus-pituitary axis); p,p'-DDE (stable metabolite of DDT; anti-androgen through competitive binding to the androgen receptor); vinclozolin (metabolites M1 and M2 act as anti-androgen; competitive binding to androgen receptor; M1 also binds weakly to the rat progesterone receptor); methoxychlor (a xeno-estrogen through α-estrogen receptor, anti-estrogen through β-estrogen receptor and an anti-androgen through androgen receptor mediated mechanism); propylthiouracil (affects the thyroid directly, causing hypothyroidism); linuron (anti-androgen; competitive binding to androgen receptor); ketoconazole (inhibits steroidogenesis in both sexes); and phenobarbital (induces P450 isoforms predominantly in the liver, accelerates metabolism of endogenous hormones and exogenous xenobiotics). The results of this study are discussed below with respect to how the protocol performed with respect to the test compounds.

Atrazine. Treatment with atrazine at 75 or 150 mg/kg/day did not affect the day of acquisition of preputial separation. Adjusted organ weights revealed an increasing trend for paired testes weight. No differences were noted in T4 or TSH levels, and no treatment-related histopathological changes were observed in the thyroid, testes, or epididymides. These results agree with those of Stoker et al. (2000), in their evaluation of the pubertal effects of atrazine (0, 12.5, 50, 100, 150, or 200 mg/kg/day) on male Wistar rats, using this study design.

p,p'-DDE. Treatment with 50 or 100 mg/kg/day p,p'-DDE significantly delayed preputial separation at both treatment levels. Adjusted thyroid, liver, and paired kidney weights were significantly increased at both doses of p,p'-DDE. With respect to reproductive tissues, adjusted paired epididymides weight exhibited a significant decrease at the high dose, whereas LABC weight exhibited a decreasing trend. Decreased T4 was observed at the high dose, whereas TSH exhibited no significant effect. No treatment-related histopathological changes were observed in the thyroid, testes, or epididymides.

Vinclozolin. The day of preputial separation exhibited significant delays at both the 30 and 100 mg/kg/day dose levels. In addition, two males in the high-dose group failed to achieve preputial separation prior to scheduled necropsy. Adjusted paired testes weight (increase), paired epididymides

(decrease), and paired seminal vesicles with coagulating glands (decrease) exhibited significant treatment-related effects at both dose levels. Adjusted dorsolateral and total prostate, and LABC weight exhibited a significant decrease at the high dose, and adjusted ventral prostate weight exhibited a decreasing trend. T4 levels were significantly decreased at both doses of vinclozolin, while no effect was observed on TSH. No treatment-related histopathological changes were observed in the thyroid, testes, or epididymides.

Methoxychlor. No effect on preputial separation was noted at either 25 or 50 mg/kg/day methoxychlor. Adjusted paired adrenal weight (increase) and seminal vesicle with coagulating glands weight (decrease) exhibited a treatment effect at the high dose. Thyroid hormones were unaffected, and no treatment-related histopathology was observed. These results are in accordance with those observed by Gray et al. (1989), who saw delayed puberty, and altered reproductive organ weights, TSH levels, and testicular histopathology at doses higher than 50 mg/kg/day, in F1 animals exposed to methoxychlor from gestation through pnd 15.

Propylthiouracil. As expected, propylthiouracil produced a decrease in circulating levels of T4 and an increase in circulating levels of TSH at both 2 and 25 mg/kg/day. Increased adjusted thyroid weight, and thyroid follicular cell hypertrophy/hyperplasia were also observed at both 2 and 25 mg/kg/day. Preputial separation was significantly delayed at the high dose. Treatment effects were also observed at both doses in the increased adjusted weights of the seminal vesicles with coagulating glands. Adjusted paired epididymides weight exhibited an increasing trend.

Ketoconazole. The postnatal day of acquisition of preputial separation was delayed at both doses of ketoconazole. Other treatment-related changes observed at both dose levels included increased adjusted liver and paired adrenal weight, and decreased adjusted seminal vesicles with coagulating glands weight. The high dose of ketoconazole also increased adjusted paired kidney weight and decreased adjusted paired testes weight. Thyroid hormone levels were not affected. No effect of treatment was observed histologically in the thyroid, testes, or epididymides.

Linuron. Linuron delayed puberty at both the 50 and 100 mg/kg/day dose levels, as evidenced by delayed acquisition of preputial separation. Adjusted liver weight exhibited a treatment effect (increase) at both dose levels; adjusted seminal vesicles with coagulating glands weight was decreased at the high dose. Both T4 and TSH levels were decreased at both dose levels, although the decrease in TSH at the high dose of linuron did not reach statistical significance. No treatment-related histopathological changes were observed in the thyroid, testes, or epididymides.

Phenobarbital. The postnatal day of acquisition of preputial separation was delayed at both doses of phenobarbital. In addition, treatment-related effects were detected at both dose levels in an increase in the adjusted weights of the thyroid and liver. A decrease in adjusted organ weight was observed at the high dose for paired testes and LABC; paired epididymides weight exhibited a decreasing

trend. No treatment related histopahtological changes were observed in the thyroid, testes, or epididymides.

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PROTOCOL DEVIATIONS

Thirty-two deviations from the protocol were noted as follows:

1. Due to an error in the breeding date of the Component 1 F0 females by Charles River Laboratories, the females were bred on August 23, 2002, instead of August 22, 2003, as requested by RTI. Thus, on the gestational forms, September 12, 2002 was gd 19 instead of gd 20 as indicated, and F0 females were checked for litters starting on gd 19 instead of gd 20.

2. Post-dosing observations were inadvertently not recorded for the following animals: Male 258 Rx Code 59969, pnd 40; Male 159 Rx Code 27489, Pnd 27; Male 177 (time and clinical observation), Rx Code 27489, pnd 45; Male 261, Rx Code 34563, pnd 31; Male 209, Rx Code 95962, pnd 40; Male 226, Rx Code 95962, pnd 39 and 40; Male 227, Rx Code 95962, pnd 40; Male 262, Rx Code 95962, pnd 41; Male 268 Rx Code 65437, pnd 41, Male 139 Rx Code 46916, pnd 41; Male 157, Rx Code 46916, pnd 30, Male 67, Rx Code 96509, pnd 23 and 26; Male 17, Rx Code 68843, pnd 29; Male 109, Rx Code 39239, pnd 34.

3. Observations were inadvertently not recorded at dosing (or on pnd 21 or 22 prior to dosing) for the following animals: Male 128, Rx 29505, pnd 22; Male 217, Rx Code 82703, pnd 21; Male 86, Rx Code 78967, pnd 47; Male 83, Rx Code 84156, Pnd 53; Male 90, Rx Code 84156, pnd 22. In addition, for Male 128, the time of observation was not recorded.

4. Post-dosing observations were done <1 hour or > 2 hours: Rx Code 82703, 5 on pnd 31, 10 on pnd 30, 3 on pnd 27, 6 on pnd 26. Rx Code 04691, 4 on pnd 23, 8 on pnd 24, 10 on pnd 25, 13 on pnd 26,15 on pnd 27, 5 on pnd 28 and 5 on pnd 30 . Rx Code 65437, 10 on pnd 23, 12 on pnd 24, 5 on pnd 25 and 5 on pnd 28, Rx Code 29505 one on pnd 23. Rx Code 15492 one on pnd 23, one on pnd 36 and two on pnd 39. Rx Code 82703, 5 on pnd 31, 9 on pnd 30, one on pnd 32. Rx Code 46916, two on pnd 46. Rx Code 78967 two on pnd 47. Rx Code 96509, one on pnd 33, Rx 68843, one on pnd 23.

5. Five males were not dosed on 11/5/02 (insufficient dosing formulation). Male 112, 115 and 130 in Rx Code 15492 on pnd 50 and Male 114 and 131 in Rx Code 07983 on pnd 50. Data from animals #115, #114, and #131 were subsequently removed from evaluation because their pnd 0 could not be established.

6. Full post-dosing samples were not available from all dosing bottles since analytical samples had to be used for dosing when insufficient dosing formulation was available. Only 1-2 ml was collected for pnd 37 and pnd 44 since the volume of dose formulation available for these days for dosing was low.

7. Page 2 of the preputial separation data form for Component 2 does did not have eartag number listed. The eartag number was available for checking on the cage card and Page 1 of preputial separation form.

8. The old food weight was inadvertently not recorded on pnd 46 for Male 3, 14, Rx Code 68843; for Male 5, 13, Rx code 39239; Male 4 Rx Code 84156; Male 6, 12, Rx Code 29505; Male 8, Rx Code 15492; Male 7, Rx Code 48266; Male 11, Rx Code 15492; Male 9, 10, Rx Code 07983. The new feed weight was inadvertently not recorded on pnd 27 for Male 21, Rx Code 48266 and on pnd 45 for Male 110, Rx Code 29505.

9. Body weight was not recorded for Male 49, Rx code 96509 on pnd 41; Male 138 body weight at sacrifice was not recorded, Rx Code 65437; weight, dose, and time of postdosing observation were not recorded for Male 108, Rx Code 84156 on pnd 32 (animal was dosed).

10. During necropsy on 11/5/02, it was noted that the adrenal glands and pituitary glands "were not being weighed immediately" as per the study protocol. When this was brought to the attention of the staff, the weigher was diligent about immediately weighing these particular organs to minimize drying out.

11. There was insufficient serum available for a sample to be transferred to EPA for Animal 267, Rx Code 46916, on 2-26-03.

12. One male pup from Dam #4 was not weighed on pnd 0 during Component 1 Lactation.

13. One male pup from Dam #52 was inadvertently not weighed on pnd 7 and one female pup from Dam #74 was not weighed on pnd 0 during Component 2 Lactation.

14. One female pup from Dam #22 that was found dead on 9-15-02, pnd 0 inadvertently did not have a necropsy performed.

15. For Male #95, Rx Code 07983, no clinical observations were recorded at dosing on pnd 51.

16. At necropsy, the prostate was excised whole, and then separated into dorsal and ventral lobes. Each lobe was weighed individually, but the two lobes were never weighed together. Instead, the computer program that was used to process the data combined the weights of the dorsal and ventral lobes to obtain the whole prostate weight. This was done to minimize handling of the tissue.

17. There is no record that the sentinel animals were selected randomly as specified in the protocol.

18. The protocol specified the approximate weight range of the pnd 21 pups as 48-55g. The actual weight of the pnd 21 animals ranged from 44-64 g.

19. Blood Collection Records: Blood collected at necropsy was split into three aliquots instead of two, as stated in the protocol.

20. Dose Formulation Records: Pnd 51 samples were to come from the 1st pnd 51, on 11/5/02. Due to a shortage of formulation they were taken from supplementary dose formulations (Rep 3 and 4) on 11/8/02 which was the second pnd 53.

21. Dose Formulation Records: Battelle formulations were not shipped with stir bars.

22. Necropsy Records, Component 1: For Male #72, Rx Code 84156, no initials/date were entered to indicate who changed the entry and when for change from Bouins fixative to formalin.

23. F1 Dosing Component 1, Notebook 1: Male 87, pnd 32 clinical observations were not conducted 1-2 hours postdosing.

24. F1 Dosing Component 1, Notebook 1: Male 49, clinical observations and body weight was not recorded on pnd 41.

25. F1 Dosing Component 1, Notebook 1: Male 14, Rx Code 68843, pnd 51, no post dose observations conducted.

26. The light cycle in ARF room 201, Component 1, was incorrect from September 5, 2002 to October 5, 2002. The light cycle was 12:12 hours (light;dark) instead of 14:10 hours (light:dark). F0 females and pups were housed in the room during this time.

27. In ARF room 201, Component 1, the humidity was above that specified in the protocol (76.7% RH) for one hour on September 17, 2002.

28. In ARF room 303, component 1, the humidity was above that specified in the protocol (87.5% RH) for one hour on October 9, 2002.

29. In ARF room 403, Component 2, the humidity was below that specified in the protocol (21.2% RH) for one hour on January 15, 2003.

30. Male 49, Rx Code 96509, was dosed (0.85 ml) on pnd 41, based on a recorded body weight 169.99 g. However, examination of the body weights for the day preceding (pnd 40, 209.40 g) and the day after (pnd 42, 230.41 g), and the fact that this animal showed steady weight gain during this portion of the study suggested that the body weight on pnd 41 had been incorrectly recorded. The body weight was not included in the analyzed data. However, since the animal was dosed on pnd 41 based on this body weight, the animal received less dosing formulation than it should have, had the weight been recorded correctly.

31. Table of Protocol Deviations for Dosing Volumes Other than that Specified in the Study Protocol. This was caused by technicians inadvertently misreading the Dosing Chart.

Male #	Rx Code	Received (ml)	Should have Received (ml)
104	78967	0.56	0.46
17	68843	0.31	0.35

32. Table of F1 Males dosed after 10:00 a.m. This was caused by some technicians taking longer to dose each animal than other technicians.

Component 1

	Rx Code						
Pnd Day	**78967**	**95509**	**68843**	**29505**	**48266**	**15492**	**07983**
24							7
25							10
26					5	11	12
27						2	2
29					1	11	10
30						2	2
32							10
33							1
34						11	10
35						10	12
36				11	12	11	12

Component 1 (continued)

	Rx Code						
Pnd Day	**78967**	**95509**	**68843**	**29505**	**48266**	**15492**	**07983**
37				2	12	13	11
38					11	3	12
39						11	12
40						13	12
41				8	14	13	12
42					1	2	12
43				6	14	11	10
44					5	13	12
45					4	13	12
46	14				1	13	12
47	15					2	2
48	1						
50	10				5	9	10
51	14	14	11	4	14	13	12
52						4	5

Component 2

	Rx Code								
Pnd Day	**27489**	**16317**	**34563**	**95962**	**82703**	**04691**	**65437**	**46916**	**59969**
28	10	10	10	9	10	10	10	10	10
29	15	15	15	15	5	5	5	5	15
30	12	15	15	15					3
31		5	15	15					
32			5	6					
33				7					
37			8	9					
38			10	15					
39		9	15	15					
40		10	14	15					
41			5	7					
42			10	9					
43			15	15					
44	1	9	15	15					
45		3	5	6					
46				1					

Component 2 (continued)

	Rx Code								
Pnd Day	**27489**	**16317**	**34563**	**95962**	**82703**	**04691**	**65437**	**46916**	**59969**
47				9					
48				5					

In the Study Director's professional opinion, these deviations did not affect the study integrity, performance, or interpretation, and are presented for completeness.

_____ _____

Julia D. George, Ph.D. Date
Study Director

Table 1-A. Analyses of Atrazine Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)	Mean % of Nominal ± RSD[e]
NA	NA	2-14-Q-M Top R-1, R1 to R3	preship	15	13.8[c]	91.8 ± 2.33
NA	NA	2-14-Q-M Bott R-1, R1 to R3	preship	15	14.0[c]	93.3 ± 1.70
NA	NA	2-14-R-M Top R-1, R1 to R3	preship	30	28.3[c]	94.3 ± 2.31
NA	NA	2-14-R-M Bott R-1, R1 to R3	preship	30	29.0[c]	96.7 ± 1.17
NA	NA	2-14-Q-M R-2, R1 to R3	preship	15	15.8[c]	105.0 ± 0.673
NA	NA	2-14-R-M R-2, R1 to R3	preship	30	30.6[c]	101.9 ± 0.771
84156	Purple	WA2-14Q-M 10-7vial	first day dosing	15	17.15[d]	114
84156	Purple	WA2-14Q-M 10-14vial	first day dosing	15	16.81[d]	112
84156	Purple	WA2-14Q-M 10-21 vial	first day dosing	15	16.85[d]	112
84156	Purple	WA2-14Q-M 10-28 vial	first day dosing	15	17.02[d]	113
39239	Brown	WA2-14R-M 10-7 vial	first day dosing	30	33.80[d]	113
39239	Brown	WA2-14R-M 10-14 vial	first day dosing	30	33.10[d]	110
39239	Brown	WA2-14R-M 10-21 vial	first day dosing	30	31.43[d]	105
39239	Brown	QA2-14R-M 10-28 vial	first day dosing	30	32.11[d]	107
84156	Purple	WA2-14-Q-M Rep3Jar	postdose	15	14.1[d]	94
39239	Brown	WA2-14-R-M Rep3Jar	postdose	30	28.8[d]	96

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.
[b] Samples were taken prior to shipping from Battelle to RTI (preship), on the first day of dosing for pnd 23, 30, 37, 44, and after dosing was completed (postdose).
[c] n = 3 for individual determinations
[d] n = 1 for individual determinations
[e] Data are presented as mean % (± % relative standard deviation).

Table 1-B. Analyses of p,p'-DDE Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)	Mean % of Nominal ± RSD[e]
NA	NA	2-14-N-M R-1 R-1 to R-3	preship	10	9.19[c]	91.9 ± 2.34[e]
NA	NA	2-14-P-M R-1 R-1 to R-3	preship	20	18.2[c]	91.0 ± 1.34
29505	Pink	2-14-N-M 10-7vial	first day dosing	10	9.30[d]	93
29505	Pink	2-14-N-M 10-14vial	first day dosing	10	9.29[d]	93
29505	Pink	2-14-N-M 10-21vial	first day dosing	10	9.34[d]	93
29505	Pink	2-14-N-M 10-28vial	first day dosing	10	9.30[d]	93
48266	Yellow	2-14-P-M 10-7vial	first day dosing	20	18.1[d]	91
48266	Yellow	2-14-P-M 10-14vial	first day dosing	20	18.2[d]	91
48266	Yellow	2-14-P-M 10-21vial	first day dosing	20	18.4[d]	92
48266	Yellow	2-14-P-M 10-28vial	first day dosing	20	–[f]	--
29505	Pink	2-14-N-M Rep3Jar	postdosing	10	9.40[d]	94
48266	Yellow	2-14-P-M Rep3Jar	postdosing	20	20.4[d]	102

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.
[b] Samples were taken prior to shipping from Battelle to RTI (preship), on the first day of dosing for pnd 23, 30, 37, 44, and after dosing was completed (postdose).
[c] n = 3 for individual determinations
[d] n = 1 for individual determinations
[e] Data are presented as mean % (± % relative standard deviation).
[f] Sample not received for analysis.

Table 1-C. Analyses of Vinclozolin Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)	Mean % of Nominal ± RSD[e]
NA	NA	2-14-J-M R-1 R-1, R-2, R-3	preship	6	5.60[c]	93.3 ± 0.9
NA	NA	2-14-K-M R-1 R-1, R-2, R-3	preship	20	18.7[c]	93.4 ± 1.2
15492	Green	WA 2-14-J-M Rep3Jar	postdose	6	5.72[d]	95.3
07983	Black	WA 2-14-K-M Rep3Jar	postdose	20	18.0[d]	90.0

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.
[b] Samples were taken prior to shipping from Battelle to RTI (preship), and after dosing was completed (postdose). No in-life samples were taken since the dosing solution was consumed.
[c] n = 3 for individual determinations
[d] n = 1 for individual determinations
[e] Data are presented as mean % (± % relative standard deviation).

Table 1-D. Analyses of Methoxychlor Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)	Mean % of Nominal ± RSD[e]
NA	NA	2-14-L-M R-1 R-1 to R-3	preship	5	4.69[c]	93.7 ± 1.54
NA	NA	2-14-M-M R-1 R-1 to R-3	preship	10	9.62[c]	96.2 ± 1.59
NA	NA	2-14-L-M R-2 R1 to R-3	preship	5	4.90[c]	97.9 ± 0.60
NA	NA	2-14-M-M R-2 R1 to R3	preship	10	9.85 [c]	98.5± 2.46
NA	NA	2-14-L-M R-3 R-1 to R-3	preship	5	5.48[c]	109.6 ± 2.21
NA	NA	2-14-M-M R-3 R-1 to R-3	preship	10	10.8[c]	108.5 ± 0.797
96509	Blue	WA2-14L-M 10-7vial	first day dosing	5	4.72[d]	94
96509	Blue	WA2-14L-M 10-14vial	first day dosing	5	4.63[d]	93
96509	Blue	WA2-14L-M 10-21vial	first day dosing	5	5.43[d]	109
96509	Blue	WA2-14L-M 10-28vial	first day dosing	5	4.52[d]	90
68843	Red	WA2-14M-M 10-7vial	first day dosing	10	9.23[d]	92
68843	Red	WA2-14M-M 10-14vial	first day dosing	10	9.85[d]	99
68843	Red	WA2-14M-M 10-21vial	first day dosing	10	9.26[d]	93
68843	Red	WA2-14M-M 10-28vial	first day dosing	10	9.12[d]	91
96509	Blue	WA2-14-L-M Rep1Jar	postdose	5	4.57[d]	91

(continued)

Table 1-D. Analyses of Methoxychlor Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)	Mean % of Nominal ± RSD[e]
96509	Blue	WA2-14-L-M Rep2Jar	postdose	5	4.70[d]	94
96509	Blue	WA2-14-L-M Rep4Jar	postdose	5	4.62[d]	92
68843	Red	WA2-14-M-M Rep1Jar	postdose	10	9.12[d]	91
68843	Red	WA2-14-M-M Rep2Jar	postdose	10	9.42[d]	94
68843	Red	WA2-14-M-M Rep4Jar	postdose	10	9.28[d]	93

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.

[b] Samples were taken prior to shipping from Battelle to RTI (preship), on the first day of dosing for pnd 23, 30, 37, 44, and after dosing was completed (postdose).

[c] n = 3 for individual determinations

[d] n = 1 for individual determinations

[e] Data are presented as mean % (± % relative standard deviation).

Table 1-E. Analyses of Propylthiouracil Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)[c]	Mean % of Nominal ± RSD[e]
NA	NA	2-14 B-M Rep1 to Rep3	preship	0.4	0.432[c]	108.0 ± 6.4
NA	NA	2-14 C-M Rep1 to Rep3	preship	5.0	4.95[c]	99.1 ± 4.9
04691	Pink	2-14 B-M 1-26-03pnd23	first day dosing	0.4	0.350[d]	88
04691	Pink	2-14 B-M 2-02-03pnd30	first day dosing	0.4	0.347[d]	87
04691	Pink	2-14 B-M 2-09-03pnd37	first day dosing	0.4	0.299[d]	75
04691	Pink	2-14 B-M 2-16-03pnd44	first day dosing	0.4	0.347[d]	87
04691	Pink	2-14 B-M 2-23-03pnd51	first day dosing	0.4	0.333[d]	83
65437	Black	2-14 C-M 1-26-03pnd23	first day dosing	5.0	4.44[d]	89
65437	Black	2-14 C-M 2-02-03pnd30	first day dosing	5.0	5.41[d]	108
65437	Black	2-14 C-M 2-09-03pnd37	first day dosing	5.0	4.82[d]	96
65437	Black	2-14 C-M 2-16-03pnd44	first day dosing	5.0	4.60[d]	92
65437	Black	2-14 C-M 2-23-03pnd51	first day dosing	5.0	4.16[d]	83
04691	Pink	WA2-14-B-M Rep3 Remainder	postdose	0.4	0.494[d]	124
65437	Black	WA2-14-C-M Rep3 Remainder	postdose	5.0	5.22[d]	104

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.

[b] Samples were taken prior to shipping from Battelle to RTI (preship), on the first day of dosing for pnd 23, 30, 37, 44, 51, and after dosing was completed (postdose).

[c] n = 3 for individual determinations

[d] n = 1 for individual determinations

[e] Data are presented as mean % (± % relative standard deviation).

Table 1-F. Analyses of Ketoconazole Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)	Mean % of Nominal ± RSD[e]
NA	NA	2-14F-M Rep1 to Rep 3	preship	10	10.6[c]	106.0 ± 2.29
NA	NA	2-14G-M Rep1 to Rep 3	preship	20	21.6[c]	108.1 ± 0.518
27489	Red	1-26 F-M	first day dosing	10	8.46[d]	85
27489	Red	2-2 F-M	first day dosing	10	8.59[d]	86
27489	Red	2-9 F-M	first day dosing	10	9.98[d]	100
27489	Red	2-16 F-M	first day dosing	10	10.1[d]	101
27489	Red	2-23 F-M	first day dosing	10	10.2[d]	102
16317	Blue	1-26 G-M	first day dosing	20	18.8[d]	94
16317	Blue	2-2 G-M	first day dosing	20	19.8[d]	99
16317	Blue	2-9 G-M	first day dosing	20	19.8[d]	99
16317	Blue	2-16 G-M	first day dosing	20	19.1[d]	96
16317	Blue	2-23 G-M	first day dosing	20	18.2[d]	91
27489	Red	Remain2-14F-M rep3	postdose	10	10.1[d]	101
16317	Blue	Remain2-14 G-M rep3	postdose	20	20.0[d]	100

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.

[b] Samples were taken prior to shipping from Battelle to RTI (preship), on the first day of dosing for pnd 23, 30, 37, 44, 51, and after dosing was completed (postdose).

[c] n = 3 for individual determinations

[d] n = 1 for individual determinations

[e] Data are presented as mean % (± % relative standard deviation).

Table 1-G. Analyses of Linuron Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)[c]	Mean % of Nominal ± RSD[e]
NA	NA	2-14-D-M R-1 to R-3	preship	10	10.5[c]	105 ± 1.81
NA	NA	2-14-E-M R-1 to R-3	preship	20	20.1[c]	101 ± 1.83
46916	Green	1-26-03 D-M	first day dosing	10	12.3[d]	123
46916	Green	2-02-03 D-M	first day dosing	10	10.2[d]	102
46916	Green	2-09-03 D-M	first day dosing	10	10.8[d]	108
46916	Green	2-16-03 D-M	first day dosing	10	9.90[d]	99
46916	Green	2-23-03 D-M	first day dosing	10	10.4[d]	104
59969	Yellow	1-26-03 E-M	first day dosing	20	19.4[d]	97
59969	Yellow	2-02-03 E-M	first day dosing	20	19.0[d]	95
59969	Yellow	2-09-03 E-M	first day dosing	20	19.7[d]	99
59969	Yellow	2-16-03 E-M	first day dosing	20	19.8[d]	99
59969	Yellow	2-23-03 E-M	first day dosing	20	21.2[d]	106
46916	Green	Rec. 2-14-D-M Rep-3	postdose	10	11.9[d]	119
59969	Yellow	Rec. 2-14-E-M Rep-3	postdose	20	19.4[d]	97

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.

[b] Samples were taken prior to shipping from Battelle to RTI (preship), on the first day of dosing for pnd 23, 30, 37, 44, 51, and after dosing was completed (postdose).

[c] n = 3 for individual determinations

[d] n = 1 for individual determinations

[e] Data are presented as mean % (± % relative standard deviation).

Table 1-H. Analyses of Phenobarbital Dose Formulations[a]

RTI Rx Code	RTI Color Code	Battelle Sample Code	Sample Type[b]	Nominal Concentration (mg/ml)	Analytical Concentration (mg/ml)	Mean % of Nominal ± RSD[e]
NA	NA	2-14 H-M R-1 to R-3	preship	10	9.64[c]	96.4 ± 0.99
NA	NA	2-14 I-M R-1 to R-3	preship	20	19.0[c]	95.0 ± 5.6
34563	Orange	1-26-03 H-M	first day dosing	10	9.40[d]	94
34563	Orange	2-02-03 H-M	first day dosing	10	9.77[d]	98
34563	Orange	2-09-03 H-M	first day dosing	10	9.92[d]	99
34563	Orange	2-16-03 H-M	first day dosing	10	10.2[d]	102
34563	Orange	2-23-03 H-M	first day dosing	10	10.3[d]	103
95962	Brown	1-26-03 I-M	first day dosing	20	19.9[d]	100
95962	Brown	2-02-03 I-M	first day dosing	20	20.5[d]	103
95962	Brown	2-09-03 I-M	first day dosing	20	19.6[d]	98
95962	Brown	2-16-03 I-M	first day dosing	20	19.7[d]	99
95962	Brown	2-23-03 I-M	first day dosing	20	19.8[d]	99
34563	Orange	Rec. 2-14-H-M Rep-3	postdose	10	10.0[d]	100
95962	Brown	Rec. 2-14-I-M Rep-3	postdose	20	20.2[d]	101

[a] Dosing solutions were formulated in corn oil vehicle for administration at 5 ml/kg.

[b] Samples were taken prior to shipping from Battelle to RTI (preship), on the first day of dosing for pnd 23, 30, 37, 44, 51, and after dosing was completed (postdose).

[c] n = 3 for individual determinations

[d] n = 1 for individual determinations

[e] Data are presented as mean % (± % relative standard deviation).

Table 2-A. Summary of the Fate of the Atrazine-Treated F_1 Males (page 1 of 1)

	Atrazine (mg/kg/day, po)		
	0	**75**	**150**
NO. OF MALES ON STUDY	12[a]	13[b]	12[c]
Phase of Study			
Post Wean Period	0	1[d]	0
Scheduled Sacrifice	12	12	12

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 18 was removed from the study because it was not dosed on the correct postnatal days and male 119 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Males 55, 118 and 127 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Male 54 was found dead on postnatal day 37 after dosing (misdirected dose).

Table 2-B. Summary of the Fate of the p,p'-Dichlorodiphenyldichloroethane-Treated F_1 Males (page 1 of 1)

	p,p'-Dichlorodiphenyldichloroethane (mg/kg/day, po)		
	0	**50**	**100**
NO. OF MALES ON STUDY	12[a]	14[b]	15
Phase of Study			
Post Wean Period	0	1[c]	0
Scheduled Sacrifice	12	13	15

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 74 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Male 20 was euthanized on postnatal day 29 after dosing due to a leg injury.

Table 2-C. Summary of the Fate of the Vinclozolin-Treated F_1 Males (page 1 of 1)

	Vinclozolin (mg/kg/day, po)		
	0	**30**	**100**
NO. OF MALES ON STUDY	12[a]	13[b]	12[c]
Phase of Study			
Post Wean Period	0	0	0
Scheduled Sacrifice	12	13	12

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 79 and 115 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Males 24, 114 and 131 were removed from the study because their correct postnatal day 0 could not be confirmed.

Table 2-D. Summary of the Fate of the Methoxychlor-Treated F_1 Males (page 1 of 1)

	Methoxychlor (mg/kg/day, po)		
	0	**25**	**50**
NO. OF MALES ON STUDY	12[a]	15	13[b]
Phase of Study			
Post Wean Period	0	0	0
Scheduled Sacrifice	12	15	13

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 17 and 30 were removed from the study because their correct postnatal day 0 could not be confirmed.

Table 2-E. Summary of the Fate of the Propylthiouracil-Treated F_1 Males (page 1 of 1)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
NO. OF MALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	1[a]	0	1[b]
Scheduled Sacrifice	14	15	14

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Male 268 was found dead on postnatal day 50 prior to dosing.

Table 2-F. Summary of the Fate of the Ketoconazole-Treated F_1 Males (page 1 of 1)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
NO. OF MALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	1[a]	0	1[b]
Scheduled Sacrifice	14	15	14

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Male 242 was found dead on postnatal day 37 prior to dosing (misdirected dose).

Table 2-G. Summary of the Fate of the Linuron-Treated F_1 Males (page 1 of 1)

	Linuron (mg/kg/day, po)		
	0	**50**	**100**
NO. OF MALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	1[a]	0	0
Scheduled Sacrifice	14	15	15

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).

Table 2-H. Summary of the Fate of the Phenobarbital-Treated F_1 Males (page 1 of 1)

	Phenobarbital (mg/kg/day, po)		
	0	**50**	**100**
NO. OF MALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	1[a]	0	0
Scheduled Sacrifice	14	15	15

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).

Table 3-A. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Atrazine Treated F_1 Males (page 1 of 5)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Males on Study	12[a]	13[b]	12[c]
Body Weight (pnd 21) (g)[d]	55.97 ± 1.74 N=12	56.75 ± 1.38 N=13	55.60 ± 1.60 N=12
Body Weight (pnd 22) (g)[d]	59.72 ± 1.80 N=12	61.35 ± 1.24 N=13	60.62 ± 1.70 N=12
Body Weight (pnd 23) (g)[d]	66.55 ± 1.93 N=12	66.85 ± 1.22 N=13	66.05 ± 1.83 N=12
Body Weight (pnd 24) (g)[d]	73.05 ‡ ± 2.07 §§ N=12	69.46 ± 1.30 N=13	66.35 * ± 1.68 N=12
Body Weight (pnd 25) (g)[d]	79.55 ‡‡ ± 2.24 §§§ N=12	74.86 ± 1.48 N=13	69.38 *** ± 1.68 N=12
Body Weight (pnd 26) (g)[d]	85.44 ‡‡ ± 2.28 §§§ N=12	80.50 ± 1.75 N=13	75.00 ** ± 1.84 N=12
Body Weight (pnd 27) (g)[d]	92.37 ‡‡ ± 2.48 §§§ N=12	86.79 ± 1.81 N=13	80.31 *** ± 2.14 N=12
Body Weight (pnd 28) (g)[d]	99.66 ‡‡ ± 2.54 §§§ N=12	93.44 ± 2.03 N=13	86.77 *** ± 2.32 N=12
Body Weight (pnd 29) (g)[d]	106.93 ‡‡ ± 2.82 §§ N=12	100.31 ± 1.93 N=13	94.55 ** ± 2.54 N=12

(continued)

Table 3-A. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Atrazine Treated F_1 Males (page 2 of 5)

	Atrazine (mg/kg/day, po)		
	0	75	150
Body Weight (pnd 30) (g)[d]	115.74 ‡‡ ± 2.98 §§§ N=12	107.99 ± 2.13 N=13	100.78 *** ± 2.70 N=12
Body Weight (pnd 31) (g)[d]	123.56 ‡‡‡ ± 3.26 §§§ N=12	113.53 * ± 2.08 N=13	107.24 *** ± 2.48 N=12
Body Weight (pnd 32) (g)[d]	132.74 ‡‡‡ ± 3.37 §§§ N=12	123.07 * ± 2.28 N=12[e]	114.69 *** ± 2.87 N=12
Body Weight (pnd 33) (g)[d]	141.91 ‡‡‡ ± 3.50 §§§ N=12	129.11 * ± 3.51 N=13	122.05 *** ± 2.97 N=12
Body Weight (pnd 34) (g)[d]	151.22 ‡‡‡ ± 3.69 §§§ N=12	138.88 * ± 2.55 N=13	130.44 *** ± 2.91 N=12
Body Weight (pnd 35) (g)[d]	160.77 ‡‡‡ ± 3.63 §§§ N=12	148.50 * ± 2.65 N=13	139.91 *** ± 3.26 N=12
Body Weight (pnd 36) (g)[d]	171.46 ‡‡‡ ± 4.05 §§§ N=12	159.61 * ± 2.62 N=13	150.41 *** ± 3.49 N=12
Body Weight (pnd 37) (g)[d]	180.49 ‡‡‡ ± 4.05 §§§ N=12	168.05 * ± 2.28 N=13	156.81 *** ± 3.05 N=12
Body Weight (pnd 38) (g)[d]	191.01 ‡‡‡ ± 4.19 §§§ N=12	175.90 ** ± 2.94 N=12[f]	163.33 *** ± 3.20 N=12

(continued)

Table 3-A. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Atrazine Treated F_1 Males (page 3 of 5)

	Atrazine (mg/kg/day, po)		
	0	75	150
Body Weight (pnd 39) (g)[d]	198.66 ‡‡‡ ± 4.16 §§§ N=12	184.72 * ± 2.67 N=12	171.74 *** ± 3.55 N=12
Body Weight (pnd 40) (g)[d]	208.02 ‡‡‡ ± 4.10 §§§ N=12	191.55 ** ± 2.98 N=12	180.58 *** ± 3.31 N=12
Body Weight (pnd 41) (g)[d]	216.01 ‡‡‡ ± 4.33 §§§ N=12	199.82 ** ± 2.82 N=12	188.87 *** ± 4.09 N=12
Body Weight (pnd 42) (g)[d]	225.72 ‡‡‡ ± 5.07 §§§ N=12	208.04 ** ± 2.89 N=12	194.09 *** ± 2.80 N=12
Body Weight (pnd 43) (g)[d]	235.65 ‡‡‡ ± 5.09 §§§ N=12	216.19 ** ± 2.73 N=12	201.09 *** ± 3.07 N=12
Body Weight (pnd 44) (g)[d]	245.61 ‡‡‡ ± 5.19 §§§ N=12	223.97 ** ± 3.12 N=12	208.63 *** ± 3.39 N=12
Body Weight (pnd 45) (g)[d]	255.20 ‡‡‡ ± 5.02 §§§ N=12	231.19 *** ± 3.28 N=12	215.20 *** ± 3.35 N=12
Body Weight (pnd 46) (g)[d]	261.60 ‡‡‡ ± 5.21 §§§ N=12	237.67 *** ± 3.13 N=12	220.62 *** ± 2.98 N=12
Body Weight (pnd 47) (g)[d]	271.36 ‡‡‡ ± 5.15 §§§ N=12	246.48 *** ± 3.46 N=12	227.08 *** ± 3.46 N=12

(continued)

Table 3-A. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Atrazine Treated F_1 Males (page 4 of 5)

	Atrazine (mg/kg/day, po)		
	0	75	150
Body Weight (pnd 48) (g)[d]	279.60 ‡‡‡ ± 5.06 §§§ N=12	253.93 *** ± 3.35 N=12	233.89 *** ± 3.50 N=12
Body Weight (pnd 49) (g)[d]	288.54 ‡‡‡ ± 5.29 §§§ N=12	262.49 *** ± 3.51 N=12	241.53 *** ± 3.82 N=12
Body Weight (pnd 50) (g)[d]	299.08 ‡‡‡ ± 5.35 §§§ N=12	270.35 *** ± 3.90 N=12	248.71 *** ± 3.86 N=12
Body Weight (pnd 51) (g)[d]	304.73 ‡‡‡ ± 5.65 §§§ N=12	275.67 *** ± 4.43 N=12	255.51 *** ± 4.22 N=12
Body Weight (pnd 52) (g)[d]	314.88 ‡‡‡ ± 5.38 §§§ N=12	282.14 *** ± 4.28 N=12	260.85 *** ± 4.10 N=12
Body Weight (pnd 53) (g)[d,g]	334.74 ‡‡‡ ± 9.48 §§§ N=5	285.69 *** ± 4.83 N=6	272.68 *** ± 8.97 N=4
Body Weight Change (pnd 21 to 23) (g)[d]	10.59 ± 0.55 N=12	10.10 ± 0.42 N=13	10.46 ± 0.44 N=12
Body Weight Change (pnd 23 to 30) (g)[d]	49.18 ‡‡‡ ± 1.65 §§§ N=12	41.14 *** ± 1.13 N=13	34.72 *** ± 1.08 N=12
Body Weight Change (pnd 30 to 37) (g)[d]	64.75 ‡‡‡ ± 1.57 §§§ N=12	60.06 * ± 1.42 N=13	56.04 *** ± 1.17 N=12

(continued)

Table 3-A. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Atrazine Treated F_1 Males (page 5 of 5)

	Atrazine (mg/kg/day, po)		
	0	75	150
Body Weight Change (pnd 37 to 44) (g)[d]			
	65.12 ‡‡‡ ± 1.72 §§§ N=12	55.80 *** ± 1.18 N=12[f]	51.82 *** ± 1.33 N=12
Body Weight Change (pnd 44 to 51) (g)[d]			
	59.12 ‡‡‡ ± 1.39 §§§ N=12	51.69 * ± 2.48 N=12	46.89 *** ± 1.40 N=12
Body Weight Change (pnd 51 to 52) (g)[d]			
	10.15 ‡‡ ± 1.07 §§§ N=12	6.47 * ± 0.63 N=12	5.34 ** ± 1.03 N=12
Body Weight Change (pnd 51 to 53) (g)[d,g]			
	16.93 ‡‡ ± 0.99 § N=5	9.45 ** ± 1.66 N=6	11.52 * ± 0.87 N=4
Body Weight Change (pnd 23 to 52) (g)[d]			
	248.32 ‡‡‡ ± 4.47 §§§ N=12	215.13 *** ± 3.56 N=12	194.80 *** ± 3.48 N=12
Body Weight Change (pnd 23 to 53) (g)[d,g]			
	263.44 ‡‡‡ ± 9.46 §§§ N=5	215.91 ** ± 4.44 N=6	201.19 *** ± 9.31 N=4

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 18 was removed from the study because it was not dosed on the correct postnatal days and male 119 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Males 55, 118 and 127 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Reported as the mean ± S.E.M.; pnd = postnatal day.
[e]Decrease in N is due to the body weight for one male inadvertently not being recorded.
[f]Male 54 was found dead on postnatal day 37 after dosing (misdirected dose).
[g]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
‡$p<0.05$; ANOVA Test.
‡‡$p<0.01$; ANOVA Test.
‡‡‡$p<0.001$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§$p<0.01$; Test for Linear Trend.
§§§$p<0.001$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.
**$p<0.01$; Dunnett's Test.
***$p<0.001$; Dunnett's Test.

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 1 of 5)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
No. of Males on Study	12[a]	14[b]	15
Body Weight (pnd 21) (g)[c]	55.97 ± 1.74 N=12	55.91 ± 1.82 N=14	56.56 ± 1.55 N=15
Body Weight (pnd 22) (g)[c]	59.72 ± 1.80 N=12	60.11 ± 1.95 N=14	59.88 ± 1.79 N=15
Body Weight (pnd 23) (g)[c]	66.55 ± 1.93 N=12	65.35 ± 2.06 N=14	65.02 ± 1.88 N=15
Body Weight (pnd 24) (g)[c]	73.05 ± 2.07 N=12	71.03 ± 2.16 N=14	70.19 ± 1.97 N=15
Body Weight (pnd 25) (g)[c]	79.55 ± 2.24 N=12	77.65 ± 2.34 N=14	76.61 ± 2.17 N=15
Body Weight (pnd 26) (g)[c]	85.44 ± 2.28 N=12	83.22 ± 2.81 N=14	83.78 ± 2.32 N=15
Body Weight (pnd 27) (g)[c]	92.37 ± 2.48 N=12	90.40 ± 2.82 N=14	89.82 ± 2.45 N=15
Body Weight (pnd 28) (g)[c]	99.66 ± 2.54 N=12	97.60 ± 3.09 N=14	97.80 ± 2.66 N=15
Body Weight (pnd 29) (g)[c]	106.93 ± 2.82 N=12	105.02 ± 3.25 N=14	106.27 ± 2.88 N=15

(continued)

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 2 of 5)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 30) (g)[c]	115.74 ± 2.98 N=12	113.98 ± 3.59 N=13[d]	114.59 ± 2.88 N=15
Body Weight (pnd 31) (g)[c]	123.56 ± 3.26 N=12	120.71 ± 3.68 N=13	121.96 ± 3.09 N=15
Body Weight (pnd 32) (g)[c]	132.74 ± 3.37 N=12	128.56 ± 4.53 N=13	131.36 ± 3.30 N=15
Body Weight (pnd 33) (g)[c]	141.91 ± 3.50 N=12	136.64 ± 4.92 N=13	141.74 ± 3.34 N=15
Body Weight (pnd 34) (g)[c]	151.22 ± 3.69 N=12	145.47 ± 5.61 N=13	150.99 ± 3.70 N=15
Body Weight (pnd 35) (g)[c]	160.77 ± 3.63 N=12	156.19 ± 4.73 N=13	160.39 ± 3.78 N=15
Body Weight (pnd 36) (g)[c]	171.46 ± 4.05 N=12	166.06 ± 4.95 N=13	170.78 ± 4.07 N=15
Body Weight (pnd 37) (g)[c]	180.49 ± 4.05 N=12	175.67 ± 4.96 N=13	179.62 ± 4.04 N=15
Body Weight (pnd 38) (g)[c]	191.01 ± 4.19 N=12	185.28 ± 5.09 N=13	190.03 ± 4.32 N=15

(continued)

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 3 of 5)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 39) (g)[C]	198.66 ± 4.16 N=12	194.61 ± 5.18 N=13	198.92 ± 4.39 N=15
Body Weight (pnd 40) (g)[C]	208.02 ± 4.10 N=12	205.72 ± 5.27 N=13	208.48 ± 4.67 N=15
Body Weight (pnd 41) (g)[C]	216.01 ± 4.33 N=12	214.61 ± 5.47 N=13	216.74 ± 4.66 N=15
Body Weight (pnd 42) (g)[C]	225.72 ± 5.07 N=12	223.49 ± 5.44 N=13	226.45 ± 4.68 N=15
Body Weight (pnd 43) (g)[C]	235.65 ± 5.09 N=12	233.89 ± 5.66 N=13	235.46 ± 4.83 N=15
Body Weight (pnd 44) (g)[C]	245.61 ± 5.19 N=12	242.14 ± 5.81 N=13	242.41 ± 4.73 N=15
Body Weight (pnd 45) (g)[C]	255.20 ± 5.02 N=12	252.36 ± 5.96 N=13	252.22 ± 5.12 N=15
Body Weight (pnd 46) (g)[C]	261.60 ± 5.21 N=12	260.74 ± 6.08 N=13	261.21 ± 4.74 N=15
Body Weight (pnd 47) (g)[C]	271.36 ± 5.15 N=12	270.30 ± 6.19 N=13	271.22 ± 5.43 N=15

(continued)

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 4 of 5)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 48) (g)[c]			
	279.60 ± 5.06 N=12	278.83 ± 6.30 N=13	279.23 ± 5.13 N=15
Body Weight (pnd 49) (g)[c]			
	288.54 ± 5.29 N=12	288.66 ± 6.35 N=13	289.71 ± 5.27 N=15
Body Weight (pnd 50) (g)[c]			
	299.08 ± 5.35 N=12	298.10 ± 7.08 N=13	298.24 ± 5.61 N=15
Body Weight (pnd 51) (g)[c]			
	304.73 ± 5.65 N=12	304.26 ± 6.90 N=13	305.53 ± 5.39 N=15
Body Weight (pnd 52) (g)[c]			
	314.88 ± 5.38 N=12	314.73 ± 7.42 N=13	310.70 ± 7.56 N=15
Body Weight (pnd 53) (g)[c,e]			
	334.74 ± 9.48 N=5	332.65 ± 7.98 N=6	337.07 ± 5.61 N=7
Body Weight Change (pnd 21 to 23) (g)[c]			
	10.59 ± 0.55 § N=12	9.45 ± 0.52 N=14	8.46 ± 0.88 N=15
Body Weight Change (pnd 23 to 30) (g)[c]			
	49.18 ± 1.65 N=12	48.19 ± 1.53 N=13[d]	49.58 ± 1.38 N=15
Body Weight Change (pnd 30 to 37) (g)[c]			
	64.75 ± 1.57 N=12	61.69 ± 2.56 N=13	65.03 ± 1.33 N=15

(continued)

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 5 of 5)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Body Weight Change (pnd 37 to 44) (g)[c]			
	65.12 ± 1.72 N=12	66.47 ± 1.75 N=13	62.80 ± 1.17 N=15
Body Weight Change (pnd 44 to 51) (g)[c]			
	59.12 ± 1.39 N=12	62.12 ± 1.59 N=13	63.12 ± 1.38 N=15
Body Weight Change (pnd 51 to 52) (g)[c]			
	10.15 ± 1.07 N=12	10.47 ± 1.41 N=13	5.17 ± 2.97 N=15
Body Weight Change (pnd 51 to 53) (g)[c,e]			
	16.93 ± 0.99 N=5	19.80 ± 1.38 N=6	20.19 ± 1.87 N=7
Body Weight Change (pnd 23 to 52) (g)[c]			
	248.32 ± 4.47 N=12	248.94 ± 5.73 N=13	245.69 ± 6.17 N=15
Body Weight Change (pnd 23 to 53) (g)[c,e]			
	263.44 ± 9.46 N=5	261.90 ± 7.65 N=6	268.59 ± 4.14 N=7

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 74 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Reported as the mean ± S.E.M.; pnd = postnatal day.
[d]Male 20 was euthanized on postnatal day 29 after dosing due to a leg injury.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[§]$p<0.05$; Test for Linear Trend.

Table 3-C. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 1 of 5)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
No. of Males on Study	12[a]	13[b]	12[c]
Body Weight (pnd 21) (g)[d]	55.97 ± 1.74 N=12	55.58 ± 1.63 N=13	55.34 ± 1.82 N=12
Body Weight (pnd 22) (g)[d]	59.72 ± 1.80 N=12	60.43 ± 1.90 N=13	59.50 ± 1.99 N=12
Body Weight (pnd 23) (g)[d]	66.55 ± 1.93 N=12	66.01 ± 1.91 N=13	65.21 ± 1.82 N=12
Body Weight (pnd 24) (g)[d]	73.05 ± 2.07 N=12	71.99 ± 2.01 N=13	69.68 ± 1.83 N=12
Body Weight (pnd 25) (g)[d]	79.55 ± 2.24 N=12	78.31 ± 2.22 N=13	76.12 ± 2.03 N=12
Body Weight (pnd 26) (g)[d]	85.44 ± 2.28 N=12	84.70 ± 2.40 N=13	82.25 ± 2.05 N=12
Body Weight (pnd 27) (g)[d]	92.37 ± 2.48 N=12	91.37 ± 2.52 N=13	88.60 ± 2.15 N=12
Body Weight (pnd 28) (g)[d]	99.66 ± 2.54 N=12	98.48 ± 2.72 N=13	95.95 ± 2.15 N=12
Body Weight (pnd 29) (g)[d]	106.93 ± 2.82 N=12	105.84 ± 2.99 N=13	103.67 ± 2.34 N=12

(continued)

Table 3-C. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 2 of 5)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Body Weight (pnd 30) (g)[d]	115.74 ± 2.98 N=12	113.98 ± 3.16 N=13	110.85 ± 2.45 N=12
Body Weight (pnd 31) (g)[d]	123.56 ± 3.26 N=12	121.98 ± 3.25 N=13	116.33 ± 3.01 N=12
Body Weight (pnd 32) (g)[d]	132.74 ± 3.37 N=12	130.86 ± 3.80 N=13	126.32 ± 2.83 N=12
Body Weight (pnd 33) (g)[d]	141.91 ± 3.50 N=12	140.94 ± 4.06 N=13	135.42 ± 2.87 N=12
Body Weight (pnd 34) (g)[d]	151.22 ± 3.69 N=12	149.96 ± 4.22 N=13	144.40 ± 2.83 N=12
Body Weight (pnd 35) (g)[d]	160.77 ± 3.63 N=12	159.63 ± 4.51 N=13	154.36 ± 3.06 N=12
Body Weight (pnd 36) (g)[d]	171.46 ± 4.05 N=12	170.17 ± 4.85 N=13	163.82 ± 3.04 N=12
Body Weight (pnd 37) (g)[d]	180.49 ± 4.05 N=12	179.79 ± 4.90 N=13	172.98 ± 3.49 N=12
Body Weight (pnd 38) (g)[d]	191.01 ± 4.19 N=12	189.75 ± 5.25 N=13	182.21 ± 3.49 N=12

(continued)

Table 3-C. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 3 of 5)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Body Weight (pnd 39) (g)[d]	198.66 ± 4.16 N=12	198.85 ± 5.39 N=13	190.57 ± 3.43 N=12
Body Weight (pnd 40) (g)[d]	208.02 ± 4.10 N=12	208.13 ± 5.79 N=13	200.41 ± 3.76 N=12
Body Weight (pnd 41) (g)[d]	216.01 ± 4.33 N=12	217.43 ± 5.72 N=13	209.99 ± 3.72 N=12
Body Weight (pnd 42) (g)[d]	225.72 ± 5.07 N=12	227.04 ± 6.04 N=13	217.93 ± 3.65 N=12
Body Weight (pnd 43) (g)[d]	235.65 ± 5.09 N=12	236.72 ± 6.17 N=13	227.33 ± 3.84 N=12
Body Weight (pnd 44) (g)[d]	245.61 ± 5.19 N=12	245.78 ± 6.37 N=13	236.10 ± 3.77 N=12
Body Weight (pnd 45) (g)[d] #	255.20 ± 5.02 N=12	255.54 ± 6.77 N=13	245.08 ± 3.85 N=12
Body Weight (pnd 46) (g)[d]	261.60 ± 5.21 N=12	263.99 ± 6.65 N=13	249.87 ± 4.62 N=12
Body Weight (pnd 47) (g)[d] #	271.36 ± 5.15 N=12	272.93 ± 7.08 N=13	261.27 ± 4.57 N=12

(continued)

Table 3-C. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 4 of 5)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Body Weight (pnd 48) (g)[d]			
#	279.60 ± 5.06 N=12	284.20 ± 7.36 N=13	270.83 ± 4.39 N=12
Body Weight (pnd 49) (g)[d]			
#	288.54 ± 5.29 N=12	293.34 ± 7.49 N=13	280.48 ± 4.61 N=12
Body Weight (pnd 50) (g)[d]			
#	299.08 ± 5.35 N=12	303.52 ± 7.70 N=13	288.76 ± 4.62 N=12
Body Weight (pnd 51) (g)[d]			
#	304.73 ± 5.65 N=12	310.12 ± 8.04 N=13	295.47 ± 4.98 N=12
Body Weight (pnd 52) (g)[d]			
#	314.88 ± 5.38 N=12	321.93 ± 8.73 N=13	306.71 ± 4.90 N=12
Body Weight (pnd 53) (g)[d,e]			
	334.74 ± 9.48 N=5	354.05 ± 6.83 N=5	324.67 ± 10.28 N=5
Body Weight Change (pnd 21 to 23) (g)[d]			
	10.59 ± 0.55 N=12	10.43 ± 0.70 N=13	9.87 ± 0.36 N=12
Body Weight Change (pnd 23 to 30) (g)[d]			
	49.18 ± 1.65 N=12	47.97 ± 1.53 N=13	45.64 ± 0.85 N=12
Body Weight Change (pnd 30 to 37) (g)[d]			
	64.75 ± 1.57 N=12	65.81 ± 1.92 N=13	62.13 ± 1.35 N=12

(continued)

Table 3-C. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 5 of 5)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Body Weight Change (pnd 37 to 44) (g)[d]			
	65.12 ± 1.72 N=12	65.99 ± 1.87 N=13	63.12 ± 1.58 N=12
Body Weight Change (pnd 44 to 51) (g)[d]			
	59.12 ± 1.39 N=12	64.34 ± 2.45 N=13	59.36 ± 1.65 N=12
Body Weight Change (pnd 51 to 52) (g)[d]			
	10.15 ± 1.07 N=12	11.80 ± 1.18 N=13	11.24 ± 1.09 N=12
Body Weight Change (pnd 51 to 53) (g)[d,e]			
	16.93 ‡‡ ± 0.99 N=5	25.60 ** ± 1.76 N=5	19.50 ± 1.26 N=5
Body Weight Change (pnd 23 to 52) (g)[d]			
#	248.32 ± 4.47 N=12	255.92 ± 7.47 N=13	241.50 ± 3.92 N=12
Body Weight Change (pnd 23 to 53) (g)[d,e]			
	263.44 ± 9.46 N=5	282.17 ± 5.84 N=5	254.82 ± 9.63 N=5

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 79 and 115 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Males 24, 114 and 131 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Reported as the mean ± S.E.M.; pnd = postnatal day.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡‡$p<0.01$; ANOVA Test.
**$p<0.01$; Dunnett's Test.

Table 3-D. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 1 of 5)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Males on Study	12[a]	15	13[b]
Body Weight (pnd 21) (g)[c]	55.97 ± 1.74 N=12	56.76 ± 1.42 N=15	56.19 ± 1.97 N=13
Body Weight (pnd 22) (g)[c]	59.72 ± 1.80 N=12	59.89 ± 1.51 N=15	60.34 ± 2.17 N=13
Body Weight (pnd 23) (g)[c]	66.55 ± 1.93 N=12	66.82 ± 1.63 N=15	66.17 ± 2.34 N=13
Body Weight (pnd 24) (g)[c]	73.05 ± 2.07 N=12	72.87 ± 1.62 N=15	72.14 ± 2.57 N=13
Body Weight (pnd 25) (g)[c]	79.55 ± 2.24 N=12	79.53 ± 1.67 N=15	79.15 ± 2.61 N=13
Body Weight (pnd 26) (g)[c]	85.44 ± 2.28 N=12	86.20 ± 1.73 N=15	85.91 ± 2.80 N=13
Body Weight (pnd 27) (g)[c]	92.37 ± 2.48 N=12	93.91 ± 1.86 N=15	93.38 ± 2.98 N=13
Body Weight (pnd 28) (g)[c]	99.66 ± 2.54 N=12	101.13 ± 1.94 N=15	100.64 ± 3.12 N=13
Body Weight (pnd 29) (g)[c]	106.93 ± 2.82 N=12	108.69 ± 2.06 N=15	108.31 ± 3.52 N=13

(continued)

Table 3-D. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 2 of 5)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Body Weight (pnd 30) (g)[C]	115.74 ± 2.98 N=12	117.32 ± 2.23 N=15	116.30 ± 3.82 N=13
Body Weight (pnd 31) (g)[C]	123.56 ± 3.26 N=12	124.03 ± 2.56 N=15	123.59 ± 3.75 N=13
Body Weight (pnd 32) (g)[C]	132.74 ± 3.37 N=12	131.67 ± 3.11 N=15	133.45 ± 4.21 N=13
Body Weight (pnd 33) (g)[C]	141.91 ± 3.50 N=12	139.93 ± 3.87 N=15	142.50 ± 4.31 N=13
Body Weight (pnd 34) (g)[C]	151.22 ± 3.69 N=12	147.86 ± 4.61 N=15	151.54 ± 4.56 N=13
Body Weight (pnd 35) (g)[C]	160.77 ± 3.63 N=12	157.03 ± 5.27 N=15	159.51 ± 4.89 N=13
Body Weight (pnd 36) (g)[C]	171.46 ± 4.05 N=12	168.99 ± 3.90 N=15	171.63 ± 5.21 N=13
Body Weight (pnd 37) (g)[C]	180.49 ± 4.05 N=12	177.91 ± 4.13 N=15	181.34 ± 5.33 N=13
Body Weight (pnd 38) (g)[C]	191.01 ± 4.19 N=12	187.92 ± 4.22 N=15	189.69 ± 5.66 N=13

(continued)

Table 3-D. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 3 of 5)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Body Weight (pnd 39) (g)[c]	198.66 ± 4.16 N=12	194.84 ± 4.43 N=15	196.72 ± 5.50 N=13
Body Weight (pnd 40) (g)[c]	208.02 ± 4.10 N=12	204.48 ± 4.23 N=15	206.99 ± 6.09 N=13
Body Weight (pnd 41) (g)[c]	216.01 ± 4.33 N=12	211.91 ± 4.42 N=14[d]	213.80 ± 6.12 N=13
Body Weight (pnd 42) (g)[c]	225.72 ± 5.07 N=12	223.36 ± 4.41 N=15	222.74 ± 6.49 N=13
Body Weight (pnd 43) (g)[c]	235.65 ± 5.09 N=12	229.15 ± 4.30 N=15	230.03 ± 6.83 N=13
Body Weight (pnd 44) (g)[c]	245.61 ± 5.19 N=12	238.17 ± 4.68 N=15	237.99 ± 6.89 N=13
Body Weight (pnd 45) (g)[c]	255.20 ± 5.02 N=12	247.69 ± 4.72 N=15	246.74 ± 6.77 N=13
Body Weight (pnd 46) (g)[c]	261.60 ± 5.21 N=12	254.35 ± 4.77 N=15	253.82 ± 7.00 N=13
Body Weight (pnd 47) (g)[c]	271.36 ± 5.15 N=12	263.46 ± 5.14 N=15	263.32 ± 6.92 N=13

(continued)

Table 3-D. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 4 of 5)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Body Weight (pnd 48) (g)[c]	279.60 ± 5.06 N=12	271.39 ± 5.05 N=15	271.68 ± 7.51 N=13
Body Weight (pnd 49) (g)[c]	288.54 ± 5.29 N=12	280.78 ± 5.23 N=15	280.25 ± 7.87 N=13
Body Weight (pnd 50) (g)[c]	299.08 ± 5.35 N=12	288.78 ± 5.12 N=15	288.24 ± 8.00 N=13
Body Weight (pnd 51) (g)[c]	304.73 ± 5.65 N=12	293.80 ± 4.86 N=15	290.44 ± 7.73 N=13
Body Weight (pnd 52) (g)[c]	314.88 ± 5.38 N=12	302.69 ± 4.91 N=15	297.93 ± 7.88 N=13
Body Weight (pnd 53) (g)[c,e]	334.74 ± 9.48 N=5	318.52 ± 4.36 N=7	328.01 ± 7.84 N=6
Body Weight Change (pnd 21 to 23) (g)[c]	10.59 ± 0.55 N=12	10.06 ± 0.44 N=15	9.97 ± 0.69 N=13
Body Weight Change (pnd 23 to 30) (g)[c]	49.18 ± 1.65 N=12	50.50 ± 1.18 N=15	50.13 ± 1.61 N=13
Body Weight Change (pnd 30 to 37) (g)[c]	64.75 ± 1.57 N=12	60.59 ± 2.66 N=15	65.04 ± 1.71 N=13

(continued)

Table 3-D. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 5 of 5)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Body Weight Change (pnd 37 to 44) (g)[c]			
	65.12 ‡‡ ± 1.72 §§ N=12	60.26 ± 1.52 N=15	56.66 ** ± 1.92 N=13
Body Weight Change (pnd 44 to 51) (g)[c]			
	59.12 ‡ ± 1.39 §§ N=12	55.63 ± 1.59 N=15	52.45 ** ± 1.45 N=13
Body Weight Change (pnd 51 to 52) (g)[c]			
	10.15 ± 1.07 N=12	8.89 ± 0.94 N=15	7.49 ± 0.78 N=13
Body Weight Change (pnd 51 to 53) (g)[c,e]			
	16.93 ± 0.99 N=5	20.43 ± 2.34 N=7	19.81 ± 2.22 N=6
Body Weight Change (pnd 23 to 52) (g)[c]			
	248.32 ± 4.47 § N=12	235.87 ± 4.20 N=15	231.76 ± 5.82 N=13
Body Weight Change (pnd 23 to 53) (g)[c,e]			
	263.44 ± 9.46 N=5	247.50 ± 4.41 N=7	256.06 ± 7.44 N=6

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 17 and 30 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Reported as the mean ± S.E.M.; pnd = postnatal day.
[d]Decrease in N is due to one body weight inadvertently not being recorded.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
‡$p<0.05$; ANOVA Test.
‡‡$p<0.01$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§$p<0.01$; Test for Linear Trend.
**$p<0.01$; Dunnett's Test.

Table 3-E. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 1 of 5)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Males on Study	15	15	15
Body Weight (pnd 21) (g)[a]			
	56.99 ± 1.32 N=15	56.72 ± 1.19 N=15	56.79 ± 1.40 N=15
Body Weight (pnd 22) (g)[a]			
	60.50 ± 1.40 N=15	60.63 ± 1.49 N=15	60.60 ± 1.46 N=15
Body Weight (pnd 23) (g)[a]			
	67.30 ± 1.41 N=15	67.16 ± 1.46 N=15	66.43 ± 1.55 N=15
Body Weight (pnd 24) (g)[a]			
	73.36 ± 1.44 N=15	74.00 ± 1.49 N=15	72.83 ± 1.43 N=15
Body Weight (pnd 25) (g)[a]			
	80.15 ± 1.69 N=15	81.52 ± 1.56 N=15	79.73 ± 1.60 N=15
Body Weight (pnd 26) (g)[a]			
	86.51 ± 1.78 N=15	88.35 ± 1.52 N=15	86.50 ± 1.72 N=15
Body Weight (pnd 27) (g)[a]			
	93.67 ± 1.93 N=15	95.56 ± 1.58 N=15	93.12 ± 1.81 N=15
Body Weight (pnd 28) (g)[a]			
	101.31 ± 2.18 N=15	103.84 ± 1.62 N=15	101.53 ± 2.13 N=15
Body Weight (pnd 29) (g)[a]			
	109.18 ± 2.24 N=15	111.47 ± 1.65 N=15	108.42 ± 2.13 N=15

(continued)

Table 3-E. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 2 of 5)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Body Weight (pnd 30) (g)[a]	117.04 ± 2.43 N=15	119.25 ± 2.01 N=15	114.81 ± 2.48 N=15
Body Weight (pnd 31) (g)[a]	124.98 ± 2.75 N=14[b]	127.87 ± 1.92 N=15	122.34 ± 2.76 N=15
Body Weight (pnd 32) (g)[a]	134.96 ± 3.19 § N=14	137.54 ± 2.09 N=15	128.81 ± 2.86 N=15
Body Weight (pnd 33) (g)[a]	144.32 ‡ ± 3.26 §§ N=14	146.63 ± 2.20 N=15	134.73 * ± 3.11 N=15
Body Weight (pnd 34) (g)[a]	153.68 ‡‡‡ ± 3.42 §§§ N=14	155.89 ± 2.34 N=15	138.99 ** ± 3.28 N=15
Body Weight (pnd 35) (g)[a]	162.40 ‡‡‡ ± 3.88 §§§ N=14	165.65 ± 2.60 N=15	144.40 *** ± 3.48 N=15
Body Weight (pnd 36) (g)[a]	172.22 ‡‡‡ ± 4.04 §§§ N=14	175.59 ± 2.79 N=15	149.05 *** ± 3.69 N=15
Body Weight (pnd 37) (g)[a]	182.68 ‡‡‡ ± 4.05 §§§ N=14	185.85 ± 2.91 N=15	153.00 *** ± 3.65 N=15
Body Weight (pnd 38) (g)[a]	192.75 ‡‡‡ ± 4.33 §§§ N=14	195.97 ± 3.35 N=15	156.71 *** ± 3.88 N=15

(continued)

Table 3-E. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 3 of 5)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Body Weight (pnd 39) (g)[a]	201.28 ‡‡‡ ± 4.33 §§§ N=14	205.33 ± 3.21 N=15	159.37 *** ± 4.02 N=15
Body Weight (pnd 40) (g)[a]	210.50 ‡‡‡ ± 4.51 §§§ N=14	214.96 ± 3.78 N=15	162.24 *** ± 4.36 N=15
Body Weight (pnd 41) (g)[a]	218.50 ‡‡‡ ± 4.31 §§§ N=14	222.46 ± 3.55 N=15	163.02 *** ± 4.12 N=15
Body Weight (pnd 42) (g)[a]	228.11 ‡‡‡ ± 4.61 §§§ N=14	230.26 ± 4.13 N=15	164.84 *** ± 4.31 N=15
Body Weight (pnd 43) (g)[a]	236.54 ‡‡‡ ± 4.88 §§§ N=14	239.19 ± 4.49 N=15	166.33 *** ± 4.26 N=15
Body Weight (pnd 44) (g)[a]	245.11 ‡‡‡ ± 5.18 §§§ N=14	246.64 ± 4.57 N=15	166.96 *** ± 4.26 N=15
Body Weight (pnd 45) (g)[a]	254.94 ‡‡‡ ± 5.18 §§§ N=14	254.76 ± 4.70 N=15	168.06 *** ± 4.27 N=15
Body Weight (pnd 46) (g)[a]	264.82 ‡‡‡ ± 5.70 §§§ N=14	262.61 ± 5.05 N=15	168.78 *** ± 4.05 N=15
Body Weight (pnd 47) (g)[a]	273.56 ‡‡‡ ± 5.58 §§§ N=14	269.14 ± 5.29 N=15	169.66 *** ± 4.15 N=15

(continued)

Table 3-E. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 4 of 5)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Body Weight (pnd 48) (g)[a]	282.57 ‡‡‡ ± 5.88 §§§ N=14	274.84 ± 5.50 N=15	169.67 *** ± 4.11 N=15
Body Weight (pnd 49) (g)[a]	292.27 ‡‡‡ ± 6.15 §§§ N=14	280.84 ± 6.38 N=15	170.22 *** ± 4.06 N=15
Body Weight (pnd 50) (g)[a]	301.88 ‡‡‡ ± 6.50 §§§ N=14	286.69 ± 6.63 N=15	171.45 *** ± 4.33 N=14[c]
Body Weight (pnd 51) (g)[a]	310.88 ‡‡‡ ± 6.60 §§§ N=14	292.97 ± 7.05 N=15	171.80 *** ± 4.49 N=14
Body Weight (pnd 52) (g)[a]	321.52 ‡‡‡ ± 6.65 §§§ N=14	297.22 * ± 7.24 N=15	172.60 *** ± 4.46 N=14
Body Weight (pnd 53) (g)[a,d]	336.44 ‡‡‡ ± 7.39 §§§ N=5	304.39 ** ± 7.07 N=5	185.14 *** ± 3.32 N=4
Body Weight Change (pnd 21 to 23) (g)[a]	10.31 ± 0.47 N=15	10.45 ± 0.48 N=15	9.64 ± 0.46 N=15
Body Weight Change (pnd 23 to 30) (g)[a]	49.74 ± 1.31 N=15	52.09 ± 0.94 N=15	48.37 ± 1.10 N=15
Body Weight Change (pnd 30 to 37) (g)[a]	65.56 ‡‡‡ ± 1.71 §§§ N=14[b]	66.60 ± 1.14 N=15	38.19 *** ± 1.57 N=15

(continued)

Table 3-E. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 5 of 5)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Body Weight Change (pnd 37 to 44) (g)[a]			
	62.43 ‡‡‡ ± 1.67 §§§ N=14	60.79 ± 2.00 N=15	13.97 *** ± 1.03 N=15
Body Weight Change (pnd 44 to 51) (g)[a]			
#	65.77 ††† ± 1.78 ŸŸŸ N=14	46.34 ÞÞÞ ± 3.58 N=15	5.27 ÞÞÞ ± 0.93 N=14[c]
Body Weight Change (pnd 51 to 52) (g)[a]			
	10.64 ‡‡‡ ± 0.57 §§§ N=14	4.24 *** ± 0.57 N=15	0.80 *** ± 0.43 N=14
Body Weight Change (pnd 51 to 53) (g)[a,d]			
	19.47 ‡‡‡ ± 2.40 §§ N=5	6.56 *** ± 1.51 N=5	-0.00 *** ± 0.44 N=4
Body Weight Change (pnd 23 to 52) (g)[a]			
	254.36 ‡‡‡ ± 5.91 §§§ N=14	230.05 ** ± 6.48 N=15	106.67 *** ± 3.35 N=14
Body Weight Change (pnd 23 to 53) (g)[a,d]			
	265.76 ‡‡‡ ± 6.58 §§§ N=5	231.96 ** ± 6.69 N=5	114.94 *** ± 3.07 N=4

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[c]Male 268 was found dead on postnatal day 50 prior to dosing.
[d]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡$p<0.05$; ANOVA Test.
‡‡‡$p<0.001$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§$p<0.01$; Test for Linear Trend.
§§§$p<0.001$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.
**$p<0.01$; Dunnett's Test.
***$p<0.001$; Dunnett's Test.
†††$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸŸ$p<0.001$; Linear trend test in robust regression model.
ÞÞÞ$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 3-F. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 1 of 5)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Body Weight (pnd 21) (g)[a]			
	56.99 ± 1.32 N=15	57.09 ± 1.33 N=15	56.56 ± 1.34 N=15
Body Weight (pnd 22) (g)[a]			
	60.50 ± 1.40 N=15	59.73 ± 1.28 N=15	59.39 ± 1.26 N=15
Body Weight (pnd 23) (g)[a]			
	67.30 ± 1.41 N=15	66.39 ± 1.64 N=15	66.39 ± 1.63 N=15
Body Weight (pnd 24) (g)[a]			
	73.36 ± 1.44 N=15	72.77 ± 1.71 N=15	71.57 ± 1.63 N=15
Body Weight (pnd 25) (g)[a]			
	80.15 ± 1.69 N=15	79.60 ± 1.81 N=15	77.68 ± 1.55 N=15
Body Weight (pnd 26) (g)[a]			
	86.51 ± 1.78 N=15	85.82 ± 1.81 N=15	83.99 ± 1.68 N=15
Body Weight (pnd 27) (g)[a]			
	93.67 ± 1.93 N=15	93.04 ± 1.95 N=15	90.59 ± 1.93 N=15
Body Weight (pnd 28) (g)[a]			
	101.31 ± 2.18 N=15	100.61 ± 2.13 N=15	97.96 ± 2.02 N=15
Body Weight (pnd 29) (g)[a]			
	109.18 ± 2.24 N=15	108.56 ± 2.28 N=15	105.42 ± 2.10 N=15

(continued)

Table 3-F. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 2 of 5)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 30) (g)[a]	117.04 ± 2.43 N=15	116.77 ± 2.45 N=15	112.87 ± 2.31 N=15
Body Weight (pnd 31) (g)[a]	124.98 ± 2.75 N=14[b]	125.24 ± 2.62 N=15	121.35 ± 2.57 N=15
Body Weight (pnd 32) (g)[a]	134.96 ± 3.19 N=14	133.74 ± 2.68 N=15	128.78 ± 2.46 N=15
Body Weight (pnd 33) (g)[a]	144.32 ± 3.26 N=14	142.68 ± 2.86 N=15	138.31 ± 3.04 N=15
Body Weight (pnd 34) (g)[a]	153.68 ± 3.42 N=14	151.41 ± 2.88 N=15	145.86 ± 2.91 N=15
Body Weight (pnd 35) (g)[a]	162.40 ± 3.88 N=14	161.64 ± 3.76 N=15	155.63 ± 3.32 N=15
Body Weight (pnd 36) (g)[a]	172.22 ± 4.04 N=14	171.30 ± 3.61 N=15	165.16 ± 3.27 N=15
Body Weight (pnd 37) (g)[a]	182.68 ± 4.05 N=14	181.94 ± 3.92 N=15	174.63 ± 3.81 N=14[c]
Body Weight (pnd 38) (g)[a]	192.75 ± 4.33 N=14	191.62 ± 4.08 N=15	183.19 ± 3.84 N=14

(continued)

Table 3-F. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 3 of 5)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 39) (g)[a]	201.28 ± 4.33 N=14	199.28 ± 4.55 N=15	192.08 ± 3.99 N=14
Body Weight (pnd 40) (g)[a]	210.50 ± 4.51 N=14	207.73 ± 4.90 N=15	200.41 ± 4.00 N=14
Body Weight (pnd 41) (g)[a]	218.50 ± 4.31 N=14	215.08 ± 4.87 N=15	207.38 ± 4.12 N=14
Body Weight (pnd 42) (g)[a]	228.11 ± 4.61 N=14	224.41 ± 5.16 N=15	216.59 ± 4.46 N=14
Body Weight (pnd 43) (g)[a]	236.54 ± 4.88 N=14	233.70 ± 5.25 N=15	225.33 ± 4.87 N=14
Body Weight (pnd 44) (g)[a]	245.11 ± 5.18 N=14	242.73 ± 5.29 N=15	233.63 ± 4.77 N=14
Body Weight (pnd 45) (g)[a]	254.94 ± 5.18 N=14	251.27 ± 5.18 N=15	241.25 ± 4.77 N=14
Body Weight (pnd 46) (g)[a]	264.82 ± 5.70 § N=14	260.47 ± 5.51 N=15	248.99 ± 5.00 N=14
Body Weight (pnd 47) (g)[a]	273.56 ± 5.58 N=14	270.20 ± 5.60 N=15	259.16 ± 5.59 N=14

(continued)

Table 3-F. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 4 of 5)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 48) (g)[a]	282.57 ± 5.88 § N=14	277.97 ± 5.36 N=15	265.32 ± 5.30 N=14
Body Weight (pnd 49) (g)[a]	292.27 ± 6.15 § N=14	288.40 ± 5.61 N=15	274.05 ± 5.84 N=14
Body Weight (pnd 50) (g)[a]	301.88 ± 6.50 N=14	298.08 ± 5.86 N=15	284.61 ± 5.84 N=14
Body Weight (pnd 51) (g)[a]	310.88 ± 6.60 N=14	308.55 ± 5.82 N=15	294.73 ± 6.21 N=14
Body Weight (pnd 52) (g)[a]	321.52 ± 6.65 N=14	321.62 ± 6.46 N=15	303.57 ± 6.56 N=14
Body Weight (pnd 53) (g)[a,d]	336.44 ± 7.39 N=5	337.44 ± 8.38 N=5	343.20 ± 5.69 N=4
Body Weight Change (pnd 21 to 23) (g)[a]	10.31 ± 0.47 N=15	9.29 ± 0.65 N=15	9.83 ± 0.59 N=15
Body Weight Change (pnd 23 to 30) (g)[a]	49.74 ± 1.31 N=15	50.39 ± 1.26 N=15	46.48 ± 0.95 N=15
Body Weight Change (pnd 30 to 37) (g)[a]	65.56 ± 1.71 N=14[b]	65.17 ± 1.69 N=15	62.21 ± 1.58 N=14[c]

(continued)

Table 3-F. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 5 of 5)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Body Weight Change (pnd 37 to 44) (g)[a]			
	62.43 ± 1.67 N=14	60.78 ± 1.90 N=15	59.00 ± 1.28 N=14
Body Weight Change (pnd 44 to 51) (g)[a]			
	65.77 ± 1.78 § N=14	65.83 ± 1.38 N=15	61.10 ± 1.62 N=14
Body Weight Change (pnd 51 to 52) (g)[a]			
	10.64 ± 0.57 N=14	13.06 ± 2.42 N=15	8.84 ± 0.96 N=14
Body Weight Change (pnd 51 to 53) (g)[a,d]			
	19.47 ± 2.40 N=5	21.67 ± 1.78 N=5	18.37 ± 3.37 N=4
Body Weight Change (pnd 23 to 52) (g)[a]			
	254.36 ± 5.91 § N=14	255.23 ± 5.45 N=15	237.51 ± 5.32 N=14
Body Weight Change (pnd 23 to 53) (g)[a,d]			
	265.76 ± 6.58 N=5	266.63 ± 7.51 N=5	272.19 ± 6.15 N=4

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[c]Male 242 was found dead on postnatal day 37 prior to dosing (misdirected dose).
[d]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
§$p<0.05$; Test for Linear Trend.

Table 3-G. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Linuron Treated F_1 Males (page 1 of 5)

	Linuron (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.99 ± 1.32 N=15	57.00 ± 1.19 N=15	57.08 ± 1.14 N=15
Body Weight (pnd 22) (g)[a]	60.50 ± 1.40 N=15	59.96 ± 1.22 N=15	59.55 ± 1.30 N=15
Body Weight (pnd 23) (g)[a]	67.30 ± 1.41 N=15	67.11 ± 1.32 N=15	65.60 ± 1.28 N=15
Body Weight (pnd 24) (g)[a]	73.36 ± 1.44 **§** N=15	71.30 ± 1.23 N=15	69.06 ± 1.46 N=15
Body Weight (pnd 25) (g)[a]	80.15 ‡ ± 1.69 **§§** N=15	77.02 ± 1.30 N=15	74.26 ***** ± 1.66 N=15
Body Weight (pnd 26) (g)[a]	86.51 ‡ ± 1.78 **§§** N=15	82.50 ± 1.45 N=15	79.28 ****** ± 1.64 N=15
Body Weight (pnd 27) (g)[a]	93.67 ‡‡ ± 1.93 **§§** N=15	88.33 ± 1.54 N=15	85.12 ****** ± 1.77 N=15
Body Weight (pnd 28) (g)[a]	101.31 ‡‡ ± 2.18 **§§** N=15	96.42 ± 1.75 N=15	92.16 ****** ± 2.05 N=15
Body Weight (pnd 29) (g)[a]	109.18 ‡‡ ± 2.24 **§§§** N=15	103.39 ± 1.79 N=15	98.43 ****** ± 2.33 N=15

(continued)

Table 3-G. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Linuron Treated F_1 Males (page 2 of 5)

	Linuron (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 30) (g)[a]	117.04 ‡‡ ± 2.43 §§§ N=15	110.51 ± 1.96 N=15	105.15 ** ± 2.38 N=15
Body Weight (pnd 31) (g)[a]	124.98 ‡‡ ± 2.75 §§§ N=14[b]	117.90 ± 2.04 N=15	111.69 *** ± 2.49 N=15
Body Weight (pnd 32) (g)[a]	134.96 ‡‡‡ ± 3.19 §§§ N=14	126.13 * ± 2.11 N=15	118.60 *** ± 2.61 N=15
Body Weight (pnd 33) (g)[a]	144.32 ‡‡‡ ± 3.26 §§§ N=14	134.44 * ± 2.30 N=15	126.46 *** ± 2.78 N=15
Body Weight (pnd 34) (g)[a]	153.68 ‡‡‡ ± 3.42 §§§ N=14	141.99 * ± 2.47 N=15	132.72 *** ± 3.00 N=15
Body Weight (pnd 35) (g)[a]	162.40 ‡‡‡ ± 3.88 §§§ N=14	151.60 * ± 2.50 N=15	142.85 *** ± 3.16 N=15
Body Weight (pnd 36) (g)[a]	172.22 ‡‡‡ ± 4.04 §§§ N=14	161.09 ± 2.64 N=15	152.01 *** ± 3.53 N=15
Body Weight (pnd 37) (g)[a]	182.68 ‡‡‡ ± 4.05 §§§ N=14	170.88 * ± 2.86 N=15	161.56 *** ± 3.75 N=15
Body Weight (pnd 38) (g)[a]	192.75 ‡‡‡ ± 4.33 §§§ N=14	179.36 * ± 2.91 N=15	168.27 *** ± 3.70 N=15

(continued)

Table 3-G. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Linuron Treated F_1 Males (page 3 of 5)

	Linuron (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 39) (g)[a]	201.28 ‡‡‡ ± 4.33 §§§ N=14	188.23 * ± 3.05 N=15	176.66 *** ± 4.12 N=15
Body Weight (pnd 40) (g)[a]	210.50 ‡‡‡ ± 4.51 §§§ N=14	197.35 * ± 3.13 N=15	183.02 *** ± 4.17 N=15
Body Weight (pnd 41) (g)[a]	218.50 ‡‡‡ ± 4.31 §§§ N=14	205.34 * ± 3.34 N=15	190.44 *** ± 4.32 N=15
Body Weight (pnd 42) (g)[a]	228.11 ‡‡‡ ± 4.61 §§§ N=14	213.74 * ± 3.56 N=15	198.40 *** ± 4.82 N=15
Body Weight (pnd 43) (g)[a]	236.54 ‡‡‡ ± 4.88 §§§ N=14	221.63 * ± 3.65 N=15	205.40 *** ± 4.88 N=15
Body Weight (pnd 44) (g)[a]	245.11 ‡‡‡ ± 5.18 §§§ N=14	230.85 ± 3.76 N=15	212.37 *** ± 5.08 N=15
Body Weight (pnd 45) (g)[a]	254.94 ‡‡‡ ± 5.18 §§§ N=14	240.82 ± 4.02 N=15	220.80 *** ± 5.29 N=15
Body Weight (pnd 46) (g)[a]	264.82 ‡‡‡ ± 5.70 §§§ N=14	249.74 ± 4.31 N=15	227.78 *** ± 5.36 N=15
Body Weight (pnd 47) (g)[a]	273.56 ‡‡‡ ± 5.58 §§§ N=14	258.03 ± 4.25 N=15	234.84 *** ± 5.32 N=15

(continued)

Table 3-G. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Linuron Treated F_1 Males (page 4 of 5)

	Linuron (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 48) (g)[a]	282.57 ‡‡‡ ± 5.88 §§§ N=14	266.82 ± 4.71 N=15	242.74 *** ± 5.72 N=15
Body Weight (pnd 49) (g)[a]	292.27 ‡‡‡ ± 6.15 §§§ N=14	275.28 ± 4.72 N=15	250.84 *** ± 5.98 N=15
Body Weight (pnd 50) (g)[a]	301.88 ‡‡‡ ± 6.50 §§§ N=14	284.04 ± 5.05 N=15	257.36 *** ± 5.97 N=15
Body Weight (pnd 51) (g)[a]	310.88 ‡‡‡ ± 6.60 §§§ N=14	292.16 ± 5.03 N=15	265.85 *** ± 6.47 N=15
Body Weight (pnd 52) (g)[a]	321.52 ‡‡‡ ± 6.65 §§§ N=14	302.24 ± 5.36 N=15	272.85 *** ± 6.68 N=15
Body Weight (pnd 53) (g)[a,c]	336.44 ± 7.39 § N=5	326.41 ± 11.06 N=5	298.53 ± 11.82 N=5
Body Weight Change (pnd 21 to 23) (g)[a]	10.31 ± 0.47 § N=15	10.12 ± 0.57 N=15	8.52 ± 0.62 N=15
Body Weight Change (pnd 23 to 30) (g)[a]	49.74 ‡‡‡ ± 1.31 §§§ N=15	43.39 ** ± 1.01 N=15	39.55 *** ± 1.64 N=15
Body Weight Change (pnd 30 to 37) (g)[a]	65.56 ‡‡‡ ± 1.71 §§§ N=14[b]	60.37 * ± 1.54 N=15	56.41 *** ± 1.44 N=15

(continued)

Table 3-G. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Linuron Treated F_1 Males (page 5 of 5)

	Linuron (mg/kg/day, po)		
	0	50	100
Body Weight Change (pnd 37 to 44) (g)[a]			
	62.43 ‡‡‡ ± 1.67 §§§ N=14	59.97 ± 1.03 N=15	50.81 *** ± 1.77 N=15
Body Weight Change (pnd 44 to 51) (g)[a]			
	65.77 ‡‡‡ ± 1.78 §§§ N=14	61.31 ± 1.70 N=15	53.48 *** ± 1.84 N=15
Body Weight Change (pnd 51 to 52) (g)[a]			
#	10.64 †† ± 0.57 ŸŸ N=14	10.08 ± 0.69 N=15	6.99 ÞÞ ± 1.06 N=15
Body Weight Change (pnd 51 to 53) (g)[a,c]			
	19.47 ± 2.40 N=5	18.73 ± 1.70 N=5	15.54 ± 2.12 N=5
Body Weight Change (pnd 23 to 52) (g)[a]			
	254.36 ‡‡‡ ± 5.91 §§§ N=14	235.13 * ± 4.51 N=15	207.24 *** ± 5.92 N=15
Body Weight Change (pnd 23 to 53) (g)[a,c]			
	265.76 ‡ ± 6.58 § N=5	255.84 ± 10.27 N=5	228.29 * ± 11.40 N=5

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[c]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡$p<0.05$; ANOVA Test.
‡‡$p<0.01$; ANOVA Test.
‡‡‡$p<0.001$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§$p<0.01$; Test for Linear Trend.
§§§$p<0.001$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.
**$p<0.01$; Dunnett's Test.
***$p<0.001$; Dunnett's Test.
††$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸ$p<0.01$; Linear trend test in robust regression model.
ÞÞ$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 3-H. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 1 of 5)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.99 ± 1.32 N=15	56.91 ± 1.22 N=15	57.44 ± 1.43 N=15
Body Weight (pnd 22) (g)[a]	60.50 ± 1.40 N=15	59.61 ± 1.30 N=15	60.10 ± 1.40 N=15
Body Weight (pnd 23) (g)[a]	67.30 ± 1.41 N=15	67.20 ± 1.53 N=15	66.82 ± 1.62 N=15
Body Weight (pnd 24) (g)[a]	73.36 ± 1.44 N=15	74.60 ± 1.53 N=15	73.76 ± 1.68 N=15
Body Weight (pnd 25) (g)[a]	80.15 ± 1.69 N=15	80.63 ± 1.50 N=15	79.11 ± 1.67 N=15
Body Weight (pnd 26) (g)[a]	86.51 ± 1.78 N=15	86.65 ± 1.70 N=15	84.31 ± 1.67 N=15
Body Weight (pnd 27) (g)[a]	93.67 ± 1.93 N=15	93.52 ± 1.85 N=15	91.22 ± 1.82 N=15
Body Weight (pnd 28) (g)[a]	101.31 ± 2.18 N=15	100.53 ± 1.90 N=15	97.43 ± 1.82 N=15
Body Weight (pnd 29) (g)[a]	109.18 ± 2.24 N=15	108.65 ± 2.11 N=15	105.14 ± 2.13 N=15

(continued)

Table 3-H. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 2 of 5)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 30) (g)[a]	117.04 ± 2.43 N=15	116.65 ± 2.24 N=15	112.38 ± 2.26 N=15
Body Weight (pnd 31) (g)[a]	124.98 ± 2.75 N=14[b]	124.64 ± 2.47 N=15	118.98 ± 2.35 N=15
Body Weight (pnd 32) (g)[a]	134.96 ± 3.19 § N=14	133.15 ± 2.80 N=15	126.63 ± 2.47 N=15
Body Weight (pnd 33) (g)[a]	144.32 ± 3.26 § N=14	141.68 ± 2.88 N=15	135.27 ± 2.90 N=15
Body Weight (pnd 34) (g)[a]	153.68 ± 3.42 § N=14	150.35 ± 2.94 N=15	143.61 ± 3.18 N=15
Body Weight (pnd 35) (g)[a]	162.40 ± 3.88 N=14	160.30 ± 3.30 N=15	153.21 ± 3.40 N=15
Body Weight (pnd 36) (g)[a]	172.22 ± 4.04 N=14	170.18 ± 3.36 N=15	162.68 ± 3.44 N=15
Body Weight (pnd 37) (g)[a]	182.68 ± 4.05 § N=14	180.67 ± 3.62 N=15	171.32 ± 3.67 N=15
Body Weight (pnd 38) (g)[a]	192.75 ± 4.33 § N=14	190.22 ± 3.68 N=15	180.49 ± 3.92 N=15

(continued)

Table 3-H. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 3 of 5)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 39) (g)[a]	201.28 ± 4.33 § N=14	200.12 ± 3.83 N=15	188.91 ± 4.11 N=15
Body Weight (pnd 40) (g)[a]	210.50 ± 4.51 N=14	209.28 ± 4.01 N=15	199.68 ± 4.64 N=15
Body Weight (pnd 41) (g)[a]	218.50 ± 4.31 N=14	217.50 ± 4.32 N=15	206.17 ± 4.58 N=15
Body Weight (pnd 42) (g)[a]	228.11 ± 4.61 N=14	227.65 ± 5.07 N=15	215.93 ± 5.00 N=15
Body Weight (pnd 43) (g)[a]	236.54 ± 4.88 N=14	236.10 ± 4.62 N=15	224.82 ± 5.14 N=15
Body Weight (pnd 44) (g)[a]	245.11 ± 5.18 N=14	244.50 ± 5.25 N=15	232.75 ± 5.11 N=15
Body Weight (pnd 45) (g)[a]	254.94 ± 5.18 N=14	253.35 ± 4.95 N=15	241.28 ± 5.43 N=15
Body Weight (pnd 46) (g)[a]	264.82 ± 5.70 N=14	262.11 ± 5.37 N=15	250.02 ± 5.44 N=15
Body Weight (pnd 47) (g)[a]	273.56 ± 5.58 N=14	270.42 ± 6.01 N=15	258.52 ± 5.60 N=15

(continued)

Table 3-H. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 4 of 5)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 48) (g)[a]	282.57 ± 5.88 N=14	277.09 ± 6.03 N=15	266.38 ± 5.80 N=15
Body Weight (pnd 49) (g)[a]	292.27 ± 6.15 § N=14	286.45 ± 6.12 N=15	274.54 ± 6.45 N=15
Body Weight (pnd 50) (g)[a]	301.88 ± 6.50 § N=14	295.67 ± 6.37 N=15	283.39 ± 6.30 N=15
Body Weight (pnd 51) (g)[a]	310.88 ± 6.60 N=14	304.69 ± 6.67 N=15	292.34 ± 6.83 N=15
Body Weight (pnd 52) (g)[a]	321.52 ± 6.65 § N=14	320.85 ± 8.08 N=15	300.43 ± 6.82 N=15
Body Weight (pnd 53) (g)[a,c]	336.44 ± 7.39 N=5	323.98 ± 17.88 N=5	329.43 ± 15.26 N=3
Body Weight Change (pnd 21 to 23) (g)[a]	10.31 ± 0.47 N=15	10.30 ± 0.55 N=15	9.39 ± 0.73 N=15
Body Weight Change (pnd 23 to 30) (g)[a]	49.74 ± 1.31 § N=15	49.45 ± 1.47 N=15	45.56 ± 1.29 N=15
Body Weight Change (pnd 30 to 37) (g)[a]	65.56 ‡ ± 1.71 §§ N=14[b]	64.02 ± 1.59 N=15	58.94 * ± 1.84 N=15

(continued)

Table 3-H. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 5 of 5)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Body Weight Change (pnd 37 to 44) (g)[a]			
	62.43 ± 1.67 N=14	63.83 ± 2.30 N=15	61.43 ± 1.86 N=15
Body Weight Change (pnd 44 to 51) (g)[a]			
	65.77 ± 1.78 § N=14	60.19 ± 1.86 N=15	59.59 ± 1.97 N=15
Body Weight Change (pnd 51 to 52) (g)[a]			
	10.64 ± 0.57 N=14	16.16 ± 6.56 N=15	8.09 ± 0.69 N=15
Body Weight Change (pnd 51 to 53) (g)[a,c]			
	19.47 ± 2.40 N=5	18.77 ± 3.58 N=5	17.36 ± 1.17 N=3
Body Weight Change (pnd 23 to 52) (g)[a]			
	254.36 ‡ ± 5.91 § N=14	253.65 ± 7.64 N=15	233.61 ± 5.83 N=15
Body Weight Change (pnd 23 to 53) (g)[a,c]			
	265.76 ± 6.58 N=5	253.20 ± 17.65 N=5	257.56 ± 14.55 N=3

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[c]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
‡p<0.05; ANOVA Test.
§p<0.05; Test for Linear Trend.
§§p<0.01; Test for Linear Trend.
*p<0.05; Dunnett's Test.

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 1 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Males on Study	12[a]	13[b]	12[c]
Feed Consumption (pnd 21 to 22) (g/day)[d]			
#	8.0 ††† ± 0.5 ŸŸŸ N=11[e]	12.1 ÞÞ ± 1.1 N=13	11.1 ÞÞÞ ± 0.6 N=12
Feed Consumption (pnd 22 to 23) (g/day)[d]			
	10.0 ‡‡ ± 0.5 § N=12	6.6 ** ± 0.8 N=12[e]	7.3 * ± 1.0 N=12
Feed Consumption (pnd 23 to 24) (g/day)[d]			
	10.7 ‡‡‡ ± 0.5 §§§ N=12	7.7 *** ± 0.3 N=12[e]	6.2 *** ± 0.4 N=12
Feed Consumption (pnd 24 to 25) (g/day)[d]			
	11.5 ‡‡‡ ± 0.4 §§§ N=12	10.7 ± 0.6 N=12[f]	8.5 *** ± 0.5 N=11[f]
Feed Consumption (pnd 25 to 26) (g/day)[d]			
	11.8 ‡‡ ± 0.4 §§§ N=12	10.8 ± 0.6 N=13	9.1 ** ± 0.5 N=11[e]
Feed Consumption (pnd 26 to 27) (g/day)[d]			
	13.6 ‡‡‡ ± 0.5 §§§ N=12	11.8 * ± 0.4 N=13	9.8 *** ± 0.6 N=12
Feed Consumption (pnd 27 to 28) (g/day)[d]			
	14.7 ‡‡ ± 0.9 §§§ N=12	13.0 ± 0.5 N=13	11.4 ** ± 0.3 N=12
Feed Consumption (pnd 28 to 29) (g/day)[d]			
	13.1 ± 0.8 N=12	13.6 ± 0.4 N=13	13.8 ± 0.5 N=12
Feed Consumption (pnd 29 to 30) (g/day)[d]			
	15.2 ‡ ± 0.6 §§ N=12	14.2 ± 0.4 N=13	13.1 ** ± 0.4 N=12

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 2 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 30 to 31) (g/day)[d]	16.1 ± 0.7 N=12	15.0 ± 0.7 N=11[f]	14.7 ± 0.4 N=12
Feed Consumption (pnd 31 to 32) (g/day)[d]	17.4 ± 0.6 N=12	15.7 ± 0.9 N=12[e]	16.4 ± 0.9 N=12
Feed Consumption (pnd 32 to 33) (g/day)[d]	17.9 ‡ ± 0.5 § N=12	15.5 ± 1.0 N=13	15.0 * ± 0.6 N=11[e]
Feed Consumption (pnd 33 to 34) (g/day)[d]	19.4 ‡ ± 0.8 §§ N=12	18.1 ± 0.5 N=12[f]	16.7 * ± 0.7 N=11[f]
Feed Consumption (pnd 34 to 35) (g/day)[d]	20.8 ± 0.7 N=12	21.1 ± 0.6 N=12[f]	19.7 ± 0.9 N=12
Feed Consumption (pnd 35 to 36) (g/day)[d]	21.2 ± 0.7 N=12	23.7 ± 0.8 N=11[e,f]	23.5 ± 1.0 N=12
Feed Consumption (pnd 36 to 37) (g/day)[d]	22.2 ‡‡‡ ± 0.5 §§§ N=12	20.2 * ± 0.7 N=13	17.9 *** ± 0.5 N=12
Feed Consumption (pnd 37 to 38) (g/day)[d]	21.3 ‡‡ ± 0.7 §§§ N=12	19.4 ± 0.5 N=12[g]	17.8 *** ± 0.6 N=11[f]
Feed Consumption (pnd 38 to 39) (g/day)[d]	22.2 ± 0.7 N=12	21.9 ± 0.4 N=11[f]	20.8 ± 0.9 N=11[e]

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 3 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 39 to 40) (g/day)[d]	23.6 ± 0.6 N=12	21.8 ± 0.6 N=12	22.6 ± 0.8 N=12
Feed Consumption (pnd 40 to 41) (g/day)[d]	24.6 ± 1.3 N=12	23.6 ± 0.7 N=12	22.1 ± 0.7 N=12
Feed Consumption (pnd 41 to 42) (g/day)[d]	23.2 ± 0.8 N=11[f]	23.5 ± 0.6 N=11[f]	22.0 ± 0.7 N=12
Feed Consumption (pnd 42 to 43) (g/day)[d]	23.0 ± 1.0 N=12	24.7 ± 0.8 N=11[f]	22.2 ± 0.8 N=11[f]
Feed Consumption (pnd 43 to 44) (g/day)[d]	25.3 ‡ ± 0.9 § N=12	22.7 * ± 0.7 N=12	22.3 * ± 0.6 N=11[e]
Feed Consumption (pnd 44 to 45) (g/day)[d]	24.3 ‡ ± 0.6 §§ N=12	22.8 ± 0.7 N=12	21.4 ** ± 0.6 N=11[f]
Feed Consumption (pnd 45 to 46) (g/day)[d]	26.1 ‡‡ ± 0.7 §§§ N=11[h]	24.1 ± 0.6 N=11[h]	21.8 *** ± 0.8 N=9[e,h]
Feed Consumption (pnd 46 to 47) (g/day)[d]	25.2 ‡‡‡ ± 0.7 §§§ N=12	24.1 ± 0.6 N=12	21.0 *** ± 0.7 N=12
Feed Consumption (pnd 47 to 48) (g/day)[d]	21.2 ± 0.6 N=12	23.1 ± 0.5 N=11[f]	21.6 ± 0.7 N=12

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 4 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 48 to 49) (g/day)[d]	24.7 ‡ ± 0.7 §§ N=12	23.4 ± 0.8 N=12	21.9 * ± 0.7 N=12
Feed Consumption (pnd 49 to 50) (g/day)[d]	25.7 ‡ ± 0.6 §§ N=12	23.7 ± 1.0 N=12	22.0 ** ± 1.0 N=12
Feed Consumption (pnd 50 to 51) (g/day)[d]	28.0 ‡‡‡ ± 0.9 §§§ N=12	22.8 *** ± 0.9 N=12	22.5 *** ± 0.8 N=12
Feed Consumption (pnd 51 to 52) (g/day)[d]	23.8 ± 0.6 N=12	24.5 ± 1.2 N=12	24.7 ± 0.8 N=12
Feed Consumption (pnd 52 to 53) (g/day)[d,i]	25.2 ‡ ± 0.8 N=5	20.2 ** ± 1.1 N=6	23.2 ± 1.1 N=4
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[d]	20.2 ‡ ± 0.4 §§ N=10[j]	19.3 ± 0.3 N=7[j]	18.6 * ± 0.2 N=5[j]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[d,i]	20.7 ± 0.8 § N=4[j]	19.3 ± 0.4 N=3[j]	18.7 ± 0.0 N=2[j]
Feed Consumption (pnd 21 to 22) (g/kg/day)[d]	137.4 ‡‡ ± 6.1 § N=11[e]	205.4 ** ± 18.5 N=13	195.1 * ± 15.7 N=12
Feed Consumption (pnd 22 to 23) (g/kg/day)[d]	158.3 ‡‡ ± 7.2 § N=12	104.6 ** ± 13.8 N=12[e]	112.0 * ± 14.3 N=12

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 5 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 23 to 24) (g/kg/day)[d]	153.0 ‡‡‡ ± 4.3 §§§ N=12	113.7 *** ± 3.5 N=12[e]	94.0 *** ± 7.4 N=12
Feed Consumption (pnd 24 to 25) (g/kg/day)[d]	150.4 ‡‡ ± 3.4 §§ N=12	148.0 ± 6.8 N=12[f]	125.3 ** ± 5.9 N=11[f]
Feed Consumption (pnd 25 to 26) (g/kg/day)[d]	143.8 ± 4.6 § N=12	138.1 ± 6.0 N=13	126.2 ± 5.7 N=11[e]
Feed Consumption (pnd 26 to 27) (g/kg/day)[d]	153.6 ‡‡ ± 5.8 §§§ N=12	141.3 ± 3.3 N=13	126.6 ** ± 6.3 N=12
Feed Consumption (pnd 27 to 28) (g/kg/day)[d]	154.2 ± 11.8 N=12	144.2 ± 4.2 N=13	136.4 ± 2.8 N=12
Feed Consumption (pnd 28 to 29) (g/kg/day)[d]	125.8 ‡‡‡ ± 6.1 §§§ N=12	140.7 * ± 3.1 N=13	151.8 *** ± 3.2 N=12
Feed Consumption (pnd 29 to 30) (g/kg/day)[d]	136.1 ± 2.9 N=12	136.3 ± 2.7 N=13	133.9 ± 2.5 N=12
Feed Consumption (pnd 30 to 31) (g/kg/day)[d]	134.4 ± 4.8 N=12	136.7 ± 6.1 N=11[f]	141.5 ± 2.0 N=12
Feed Consumption (pnd 31 to 32) (g/kg/day)[d]	135.7 ± 3.5 N=12	132.6 ± 6.8 N=12[e]	147.4 ± 5.6 N=12

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 6 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 32 to 33) (g/kg/day)[d]			
	130.2 ± 2.9 N=12	119.6 ± 7.3 N=12[k]	127.2 ± 4.7 N=11[e]
Feed Consumption (pnd 33 to 34) (g/kg/day)[d]			
	132.0 ± 3.3 N=12	135.7 ± 3.6 N=12[f]	132.0 ± 3.8 N=11[f]
Feed Consumption (pnd 34 to 35) (g/kg/day)[d]			
	133.0 ‡ ± 3.4 § N=12	147.0 * ± 3.7 N=12[f]	145.0 ± 4.7 N=12
Feed Consumption (pnd 35 to 36) (g/kg/day)[d]			
	127.8 ‡‡‡ ± 4.0 §§§ N=12	154.8 *** ± 5.4 N=11[e,f]	161.6 *** ± 5.0 N=12
Feed Consumption (pnd 36 to 37) (g/kg/day)[d]			
	126.6 ± 4.2 N=12	123.0 ± 3.7 N=13	117.4 ± 5.3 N=12
Feed Consumption (pnd 37 to 38) (g/kg/day)[d]			
	114.3 ± 2.2 N=12	113.0 ± 2.1 N=12[g]	111.8 ± 2.9 N=11[f]
Feed Consumption (pnd 38 to 39) (g/kg/day)[d]			
	113.9 ‡ ± 2.4 § N=12	122.1 ± 2.6 N=11[f]	124.7 * ± 3.6 N=11[e]
Feed Consumption (pnd 39 to 40) (g/kg/day)[d]			
	116.3 ‡ ± 2.6 § N=12	115.9 ± 3.5 N=12	128.7 * ± 4.3 N=12
Feed Consumption (pnd 40 to 41) (g/kg/day)[d]			
	115.4 ± 4.4 N=12	120.6 ± 3.0 N=12	119.2 ± 2.1 N=12

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 7 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 41 to 42) (g/kg/day)[d]			
	106.7 ± 4.3 N=11[f]	115.7 ± 2.3 N=11[f]	115.2 ± 4.6 N=12
Feed Consumption (pnd 42 to 43) (g/kg/day)[d]			
	99.5 ‡‡ ± 3.9 § N=12	116.8 ** ± 3.9 N=11[f]	112.6 * ± 3.2 N=11[f]
Feed Consumption (pnd 43 to 44) (g/kg/day)[d]			
	105.6 ± 5.0 N=12	103.0 ± 2.8 N=12	109.3 ± 2.5 N=11[e]
Feed Consumption (pnd 44 to 45) (g/kg/day)[d]			
	97.5 ± 2.6 N=12	100.2 ± 2.5 N=12	101.5 ± 2.4 N=11[f]
Feed Consumption (pnd 45 to 46) (g/kg/day)[d]			
	100.2 ± 2.4 N=11[h]	101.6 ± 2.5 N=11[h]	98.5 ± 3.4 N=9[e,h]
Feed Consumption (pnd 46 to 47) (g/kg/day)[d]			
	94.7 ± 2.3 N=12	99.7 ± 2.2 N=12	93.9 ± 2.6 N=12
Feed Consumption (pnd 47 to 48) (g/kg/day)[d]			
	77.3 ‡‡‡ ± 3.1 §§§ N=12	92.8 *** ± 2.0 N=11[f]	93.5 *** ± 2.9 N=12
Feed Consumption (pnd 48 to 49) (g/kg/day)[d]			
	87.1 ± 1.9 N=12	90.8 ± 3.0 N=12	92.1 ± 2.1 N=12
Feed Consumption (pnd 49 to 50) (g/kg/day)[d]			
	87.8 ± 2.3 N=12	88.7 ± 3.1 N=12	89.9 ± 3.7 N=12

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 8 of 9)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 50 to 51) (g/kg/day)[d]			
	92.7 ‡ ± 2.6 N=12	83.2 * ± 2.6 N=12	89.2 ± 2.5 N=12
Feed Consumption (pnd 51 to 52) (g/kg/day)[d]			
	77.1 ‡‡‡ ± 2.0 §§§ N=12	87.7 * ± 3.5 N=12	95.4 *** ± 1.9 N=12
Feed Consumption (pnd 52 to 53) (g/kg/day)[d,i]			
	76.4 ‡ ± 1.5 N=5	71.0 ± 3.9 N=6	86.6 ± 1.5 N=4
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[d]			
	108.3 ‡‡ ± 1.1 §§ N=10[j]	112.5 * ± 1.3 N=7[j]	113.8 * ± 0.8 N=5[j]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[d,i]			
	104.5 ‡‡ ± 0.8 §§ N=4[j]	109.3 * ± 1.0 N=3[j]	111.1 ** ± 1.2 N=2[j]

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine Treated F_1 Males (page 9 of 9)

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 18 was removed from the study because it was not dosed on the correct postnatal days and male 119 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Males 55, 118 and 127 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Reported as the mean ± S.E.M.; pnd = postnatal day.
[e]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[f]Decrease in N is due to the feed consumption value for one or more animals being statistical outliers and therefore they were excluded.
[g]Male 54 was found dead on postnatal day 37 after dosing (misdirected dose).
[h]Decrease in N is due to one or more feed weights inadvertently not being recorded.
[i]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[j]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[k]Decrease in N is due to the postnatal day 32 body weight for one male inadvertently not being recorded.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[†††]$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
[ŸŸŸ]$p<0.001$; Linear trend test in robust regression model.
[Þ]$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
[ÞÞÞ]$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.
[‡]$p<0.05$; ANOVA Test.
[‡‡]$p<0.01$; ANOVA Test.
[‡‡‡]$p<0.001$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[§§]$p<0.01$; Test for Linear Trend.
[§§§]$p<0.001$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.
[**]$p<0.01$; Dunnett's Test.
[***]$p<0.001$; Dunnett's Test.

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 1 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
No. of Males on Study	12[a]	14[b]	15
Feed Consumption (pnd 21 to 22) (g/day)[c]			
	8.0 ± 0.5 N=11[d]	10.3 ± 0.6 N=14	9.5 ± 0.7 N=15
Feed Consumption (pnd 22 to 23) (g/day)[c]			
	10.0 ‡ ± 0.5 § N=12	7.2 * ± 0.8 N=14	7.7 * ± 0.6 N=15
Feed Consumption (pnd 23 to 24) (g/day)[c]			
	10.7 ‡ ± 0.5 § N=12	10.5 ± 0.3 N=13[e]	9.5 * ± 0.4 N=15
Feed Consumption (pnd 24 to 25) (g/day)[c]			
	11.5 ± 0.4 N=12	12.0 ± 0.4 N=14	11.3 ± 0.4 N=15
Feed Consumption (pnd 25 to 26) (g/day)[c]			
	11.8 ± 0.4 N=12	11.8 ± 0.3 N=13[e]	12.1 ± 0.4 N=15
Feed Consumption (pnd 26 to 27) (g/day)[c]			
	13.6 ‡ ± 0.5 §§ N=12	12.6 ± 0.4 N=14	11.9 * ± 0.4 N=15
Feed Consumption (pnd 27 to 28) (g/day)[c]			
	14.7 ± 0.9 N=12	13.3 ± 0.5 N=14	13.3 ± 0.5 N=14[f]
Feed Consumption (pnd 28 to 29) (g/day)[c]			
	13.1 ‡ ± 0.8 § N=12	14.6 ± 0.5 N=14	15.4 * ± 0.5 N=15
Feed Consumption (pnd 29 to 30) (g/day)[c]			
	15.2 ± 0.6 N=12	14.2 ± 0.4 N=13[g]	14.6 ± 0.4 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 2 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 30 to 31) (g/day)[c]			
	16.1 ± 0.7 N=12	15.6 ± 0.7 N=13	16.2 ± 0.5 N=15
Feed Consumption (pnd 31 to 32) (g/day)[c]			
	17.4 ± 0.6 N=12	16.0 ± 1.2 N=12[d]	18.4 ± 0.6 N=15
Feed Consumption (pnd 32 to 33) (g/day)[c]			
	17.9 ‡ ± 0.5 N=12	15.4 ± 1.2 N=12[e]	18.4 ± 0.4 N=15
Feed Consumption (pnd 33 to 34) (g/day)[c]			
	19.4 ± 0.8 N=12	17.2 ± 1.4 N=13	19.5 ± 0.7 N=15
Feed Consumption (pnd 34 to 35) (g/day)[c]			
	20.8 ± 0.7 N=12	20.0 ± 0.6 N=12[e]	20.6 ± 0.5 N=15
Feed Consumption (pnd 35 to 36) (g/day)[c]			
	21.2 ± 0.7 § N=12	23.4 ± 1.1 N=13	24.2 ± 0.8 N=15
Feed Consumption (pnd 36 to 37) (g/day)[c]			
	22.2 ± 0.5 N=12	22.2 ± 0.7 N=13	22.8 ± 0.6 N=15
Feed Consumption (pnd 37 to 38) (g/day)[c]			
	21.3 ± 0.7 N=12	21.3 ± 0.5 N=13	23.1 ± 0.8 N=15
Feed Consumption (pnd 38 to 39) (g/day)[c]			
	22.2 ± 0.7 § N=12	23.6 ± 0.9 N=13	24.7 ± 0.7 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 3 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 39 to 40) (g/day)[c]	23.6 ± 0.6 § N=12	24.9 ± 0.7 N=13	25.6 ± 0.7 N=15
Feed Consumption (pnd 40 to 41) (g/day)[c]	24.6 ± 1.3 N=12	25.4 ± 0.6 N=13	25.0 ± 0.5 N=15
Feed Consumption (pnd 41 to 42) (g/day)[c]	23.2 ‡ ± 0.8 §§ N=11[e]	24.4 ± 0.5 N=13	26.1 * ± 0.7 N=15
Feed Consumption (pnd 42 to 43) (g/day)[c]	23.0 ‡ ± 1.0 § N=12	25.5 ± 0.7 N=13	26.1 * ± 0.8 N=14[e]
Feed Consumption (pnd 43 to 44) (g/day)[c]	25.3 ± 0.9 N=12	25.1 ± 0.5 N=13	24.5 ± 0.5 N=14[e]
Feed Consumption (pnd 44 to 45) (g/day)[c]	24.3 ± 0.6 N=12	25.3 ± 0.7 N=12[e]	26.0 ± 0.7 N=14[d]
Feed Consumption (pnd 45 to 46) (g/day)[c]	26.1 ± 0.7 N=11[f]	25.8 ± 0.7 N=9[d,f]	27.4 ± 0.6 N=14[f]
Feed Consumption (pnd 46 to 47) (g/day)[c]	25.2 ± 0.7 N=12	25.1 ± 0.8 N=13	25.7 ± 0.9 N=15
Feed Consumption (pnd 47 to 48) (g/day)[c]	21.2 ‡‡‡ ± 0.6 §§§ N=12	24.4 ** ± 0.8 N=13	24.9 *** ± 0.6 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 4 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 48 to 49) (g/day)[c]			
	24.7 ± 0.7 § N=12	26.1 ± 0.7 N=13	27.0 ± 0.6 N=15
Feed Consumption (pnd 49 to 50) (g/day)[c]			
	25.7 ± 0.6 N=12	26.2 ± 1.0 N=13	27.9 ± 0.9 N=15
Feed Consumption (pnd 50 to 51) (g/day)[c]			
	28.0 ‡‡‡ ± 0.9 §§§ N=12	28.8 ± 1.2 N=13	33.4 *** ± 0.7 N=15
Feed Consumption (pnd 51 to 52) (g/day)[c]			
	23.8 ‡‡ ± 0.6 N=12	29.0 ** ± 1.3 N=13	26.0 ± 0.8 N=14[e]
Feed Consumption (pnd 52 to 53) (g/day)[c,h]			
	25.2 ± 0.8 N=5	27.6 ± 1.2 N=6	28.7 ± 1.4 N=7
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[c]			
	20.2 ‡ ± 0.4 § N=10[i]	21.3 ± 0.5 N=8[i]	21.6 * ± 0.4 N=13[i]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[c,h]			
	20.7 ± 0.8 N=4[i]	21.4 ± 0.9 N=3[i]	22.3 ± 0.4 N=7
Feed Consumption (pnd 21 to 22) (g/kg/day)[c]			
	137.4 ‡ ± 6.1 N=11[d]	179.4 * ± 13.4 N=14	162.6 ± 10.2 N=15
Feed Consumption (pnd 22 to 23) (g/kg/day)[c]			
	158.3 ± 7.2 N=12	115.0 ± 16.0 N=14	125.0 ± 11.1 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 5 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 23 to 24) (g/kg/day)[c]			
	153.0 ‡ ± 4.3 §§ N=12	151.7 ± 2.3 N=13[e]	140.0 * ± 3.6 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[c]			
	150.4 ‡ ± 3.4 N=12	161.4 * ± 2.4 N=14	154.3 ± 2.9 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[c]			
	143.8 ± 4.6 N=12	145.8 ± 5.1 N=13[e]	152.4 ± 5.9 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[c]			
	153.6 ‡ ± 5.8 § N=12	146.2 ± 4.1 N=14	137.9 * ± 3.0 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[c]			
	154.2 ± 11.8 N=12	142.4 ± 5.5 N=14	142.5 ± 2.8 N=14[f]
Feed Consumption (pnd 28 to 29) (g/kg/day)[c]			
	125.8 ‡‡‡ ± 6.1 §§§ N=12	144.5 ** ± 2.2 N=14	150.8 *** ± 2.7 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[c]			
	136.1 ± 2.9 N=12	129.7 ± 3.2 N=13[g]	133.3 ± 3.9 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[c]			
	134.4 ± 4.8 N=12	132.5 ± 4.1 N=13	137.0 ± 2.1 N=15
Feed Consumption (pnd 31 to 32) (g/kg/day)[c]			
	135.7 ‡ ± 3.5 N=12	127.1 ± 6.9 N=12[d]	145.0 ± 3.3 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 6 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 32 to 33) (g/kg/day)[c]			
	130.2 ‡ ± 2.9 N=12	115.0 ± 7.2 N=12[e]	135.6 ± 3.5 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[c]			
	132.0 ± 3.3 N=12	121.0 ± 9.7 N=13	132.7 ± 2.6 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[c]			
	133.0 ± 3.4 N=12	130.9 ± 3.2 N=12[e]	132.7 ± 3.4 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[c]			
	127.8 ‡ ± 4.0 § N=12	145.6 * ± 6.5 N=13	145.8 * ± 3.3 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[c]			
	126.6 ± 4.2 N=12	130.7 ± 3.7 N=13	130.2 ± 1.8 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[c]			
	114.3 ‡ ± 2.2 § N=12	118.8 ± 3.4 N=13	124.7 * ± 2.6 N=15
Feed Consumption (pnd 38 to 39) (g/kg/day)[c]			
	113.9 ‡‡ ± 2.4 §§ N=12	123.7 * ± 2.8 N=13	126.9 ** ± 2.5 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[c]			
	116.3 ‡‡ ± 2.6 §§ N=12	124.7 * ± 2.0 N=13	125.4 ** ± 1.7 N=15
Feed Consumption (pnd 40 to 41) (g/kg/day)[c]			
	115.4 ± 4.4 N=12	121.0 ± 2.3 N=13	118.0 ± 2.6 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 7 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 41 to 42) (g/kg/day)[c]			
	106.7 ‡ ± 4.3 § N=11[e]	111.9 ± 2.7 N=13	118.0 * ± 2.4 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[c]			
	99.5 ‡ ± 3.9 § N=12	111.9 * ± 2.8 N=13	111.7 * ± 3.5 N=14[e]
Feed Consumption (pnd 43 to 44) (g/kg/day)[c]			
	105.6 ± 5.0 N=12	105.7 ± 2.1 N=13	101.3 ± 2.0 N=14[e]
Feed Consumption (pnd 44 to 45) (g/kg/day)[c]			
	97.5 ± 2.6 N=12	102.7 ± 2.8 N=12[e]	103.7 ± 1.9 N=14[d]
Feed Consumption (pnd 45 to 46) (g/kg/day)[c]			
	100.2 ± 2.4 N=11[f]	97.2 ± 2.7 N=9[d,f]	105.7 ± 3.2 N=14[f]
Feed Consumption (pnd 46 to 47) (g/kg/day)[c]			
	94.7 ± 2.3 N=12	94.9 ± 3.5 N=13	96.6 ± 2.7 N=15
Feed Consumption (pnd 47 to 48) (g/kg/day)[c]			
	77.3 ‡‡ ± 3.1 §§ N=12	89.2 ** ± 2.9 N=13	90.5 ** ± 1.8 N=15
Feed Consumption (pnd 48 to 49) (g/kg/day)[c]			
#	87.1 †† ± 1.9 ŸŸŸ N=12	92.3 ± 2.5 N=13	94.8 ÞÞ ± 1.3 N=15
Feed Consumption (pnd 49 to 50) (g/kg/day)[c]			
	87.8 ± 2.3 § N=12	89.1 ± 2.5 N=13	94.7 ± 2.1 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 8 of 9)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 50 to 51) (g/kg/day)[c]	92.7 ‡‡‡ ± 2.6 §§§ N=12	95.7 ± 3.2 N=13	110.8 *** ± 1.7 N=15
Feed Consumption (pnd 51 to 52) (g/kg/day)[c]	77.1 ‡‡‡ ± 2.0 N=12	93.7 *** ± 3.6 N=13	83.2 ± 2.3 N=14[e]
Feed Consumption (pnd 52 to 53) (g/kg/day)[c,h]	76.4 ± 1.5 § N=5	84.3 ± 2.3 N=6	86.7 ± 3.6 N=7
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[c]	108.3 ‡‡ ± 1.1 §§§ N=10[i]	111.6 ± 1.7 N=8[i]	115.4 ** ± 1.3 N=13[i]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[c,h]	104.5 ‡‡ ± 0.8 §§§ N=4[i]	107.1 ± 1.3 N=3[i]	112.9 *** ± 1.2 N=7

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 9 of 9)

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 74 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Reported as the mean $\pm$ S.E.M.; pnd = postnatal day.
[d]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[e]Decrease in N is due to the feed consumption value for one animal being a statistical outlier and therefore it was excluded.
[f]Decrease in N is due to one or more feed weights inadvertently not being recorded.
[g]Male 20 was euthanized on postnatal day 29 after dosing due to a leg injury.
[h]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[i]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[‡]$p<0.05$; ANOVA Test.
[‡‡]$p<0.01$; ANOVA Test.
[‡‡‡]$p<0.001$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[§§]$p<0.01$; Test for Linear Trend.
[§§§]$p<0.001$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.
[**]$p<0.01$; Dunnett's Test.
[***]$p<0.001$; Dunnett's Test.
[††]$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
[ŸŸŸ]$p<0.001$; Linear trend test in robust regression model.
[ÞÞ]$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 1 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
No. of Males on Study	12[a]	13[b]	12[c]
Feed Consumption (pnd 21 to 22) (g/day)[d]			
	8.0 ± 0.5 N=11[e]	9.4 ± 0.6 N=13	8.8 ± 0.6 N=12
Feed Consumption (pnd 22 to 23) (g/day)[d]			
	10.0 ± 0.5 N=12	8.4 ± 0.6 N=13	8.5 ± 0.3 N=11[f]
Feed Consumption (pnd 23 to 24) (g/day)[d]			
	10.7 ± 0.5 N=12	10.1 ± 0.4 N=13	9.5 ± 0.3 N=12
Feed Consumption (pnd 24 to 25) (g/day)[d]			
	11.5 ± 0.4 N=12	11.9 ± 0.5 N=13	12.1 ± 0.4 N=12
Feed Consumption (pnd 25 to 26) (g/day)[d]			
	11.8 ± 0.4 N=12	12.4 ± 0.4 N=13	12.9 ± 0.3 N=12
Feed Consumption (pnd 26 to 27) (g/day)[d]			
	13.6 ± 0.5 § N=12	12.6 ± 0.5 N=13	12.1 ± 0.3 N=12
Feed Consumption (pnd 27 to 28) (g/day)[d]			
#	14.7 †† ± 0.9 N=12	12.5 Þ ± 0.3 N=12[f]	13.8 ± 0.4 N=12
Feed Consumption (pnd 28 to 29) (g/day)[d]			
	13.1 ± 0.8 N=12	15.1 ± 0.7 N=13	15.1 ± 0.4 N=12
Feed Consumption (pnd 29 to 30) (g/day)[d]			
	15.2 ± 0.6 N=12	14.7 ± 0.6 N=13	15.3 ± 0.7 N=12

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 2 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Feed Consumption (pnd 30 to 31) (g/day)[d]			
	16.1 ± 0.7 N=12	16.3 ± 0.7 N=13	17.2 ± 0.9 N=12
Feed Consumption (pnd 31 to 32) (g/day)[d]			
	17.4 ± 0.6 N=12	17.9 ± 0.8 N=13	17.9 ± 0.5 N=12
Feed Consumption (pnd 32 to 33) (g/day)[d]			
	17.9 ± 0.5 N=12	17.1 ± 0.6 N=13	16.7 ± 0.5 N=11[f]
Feed Consumption (pnd 33 to 34) (g/day)[d]			
	19.4 ± 0.8 N=12	18.0 ± 0.7 N=13	18.0 ± 0.5 N=12
Feed Consumption (pnd 34 to 35) (g/day)[d]			
#	20.8 ± 0.7 N=12	19.5 ± 0.9 N=13	19.2 ± 0.3 N=12
Feed Consumption (pnd 35 to 36) (g/day)[d]			
	21.2 ± 0.7 N=12	23.8 ± 1.1 N=13	21.9 ± 0.5 N=12
Feed Consumption (pnd 36 to 37) (g/day)[d]			
	22.2 ± 0.5 N=12	22.6 ± 0.8 N=13	22.1 ± 0.4 N=12
Feed Consumption (pnd 37 to 38) (g/day)[d]			
	21.3 ± 0.7 N=12	21.3 ± 0.7 N=13	21.5 ± 0.5 N=11[f]
Feed Consumption (pnd 38 to 39) (g/day)[d]			
	22.2 ± 0.7 N=12	24.0 ± 1.0 N=13	22.6 ± 0.6 N=12

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 3 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Feed Consumption (pnd 39 to 40) (g/day)[d]			
#	23.6 ± 0.6 N=12	25.1 ± 1.0 N=13	24.4 ± 0.5 N=12
Feed Consumption (pnd 40 to 41) (g/day)[d]			
	24.6 ± 1.3 N=12	24.4 ± 0.8 N=13	24.1 ± 0.6 N=12
Feed Consumption (pnd 41 to 42) (g/day)[d]			
	23.2 ± 0.8 N=11[f]	24.9 ± 0.9 N=12[f]	24.4 ± 0.6 N=12
Feed Consumption (pnd 42 to 43) (g/day)[d]			
	23.0 ± 1.0 N=12	24.1 ± 1.2 N=13	25.0 ± 0.6 N=11[f]
Feed Consumption (pnd 43 to 44) (g/day)[d]			
	25.3 ± 0.9 N=12	25.6 ± 0.7 N=13	24.8 ± 0.5 N=11[f]
Feed Consumption (pnd 44 to 45) (g/day)[d]			
	24.3 ± 0.6 N=12	24.6 ± 0.9 N=13	24.4 ± 0.5 N=12
Feed Consumption (pnd 45 to 46) (g/day)[d]			
	26.1 ± 0.7 § N=11[g]	24.5 ± 2.1 N=11[g]	21.5 ± 1.0 N=10[g]
Feed Consumption (pnd 46 to 47) (g/day)[d]			
#	25.2 ± 0.7 N=12	23.7 ± 1.3 N=13	23.4 ± 0.7 N=12
Feed Consumption (pnd 47 to 48) (g/day)[d]			
	21.2 ‡‡‡ ± 0.6 § N=12	25.3 *** ± 0.8 N=13	24.4 ** ± 0.6 N=12

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 4 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Feed Consumption (pnd 48 to 49) (g/day)[d]			
	24.7 ± 0.7 N=12	25.5 ± 1.1 N=13	24.9 ± 0.6 N=12
Feed Consumption (pnd 49 to 50) (g/day)[d]			
#	25.7 ± 0.6 N=12	28.1 ± 1.4 N=13	25.8 ± 0.6 N=12
Feed Consumption (pnd 50 to 51) (g/day)[d]			
	28.0 ± 0.9 N=12	31.3 ± 1.5 N=13	28.4 ± 0.9 N=12
Feed Consumption (pnd 51 to 52) (g/day)[d]			
#	23.8 ††	27.6 ÞÞ	26.0 ÞÞ
	± 0.6 N=12	± 1.2 N=13	± 0.5 N=12
Feed Consumption (pnd 52 to 53) (g/day)[d,h]			
	25.2 ± 0.8 N=5	27.0 ± 1.4 N=5	23.2 ± 1.5 N=5
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[d]			
	20.2 ± 0.4 N=10[i]	20.8 ± 0.7 N=9[i]	20.7 ± 0.3 N=7[i]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[d,h]			
	20.7 ± 0.8 N=4[i]	21.5 ± 0.8 N=3[i]	21.5 ± 0.6 N=3[i]
Feed Consumption (pnd 21 to 22) (g/kg/day)[d]			
	137.4 ± 6.1 N=11[e]	159.4 ± 6.9 N=13	152.6 ± 9.7 N=12
Feed Consumption (pnd 22 to 23) (g/kg/day)[d]			
	158.3 ± 7.2 N=12	135.5 ± 10.8 N=13	137.9 ± 9.3 N=11[f]

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 5 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Feed Consumption (pnd 23 to 24) (g/kg/day)[d]			
	153.0 ± 4.3 **§** N=12	146.4 ± 3.6 N=13	141.5 ± 3.4 N=12
Feed Consumption (pnd 24 to 25) (g/kg/day)[d]			
	150.4 **‡** ± 3.4 **§§** N=12	158.2 ± 3.8 N=13	166.4 ** ± 4.2 N=12
Feed Consumption (pnd 25 to 26) (g/kg/day)[d]			
	143.8 **‡‡** ± 4.6 **§§§** N=12	152.5 ± 2.7 N=13	163.9 ** ± 4.2 N=12
Feed Consumption (pnd 26 to 27) (g/kg/day)[d]			
	153.6 ± 5.8 N=12	142.7 ± 3.9 N=13	142.4 ± 4.8 N=12
Feed Consumption (pnd 27 to 28) (g/kg/day)[d]			
	154.2 ± 11.8 N=12	133.5 ± 2.1 N=12[f]	149.9 ± 4.4 N=12
Feed Consumption (pnd 28 to 29) (g/kg/day)[d]			
	125.8 **‡‡‡** ± 6.1 **§§** N=12	146.9 ** ± 3.2 N=13	151.2 *** ± 3.1 N=12
Feed Consumption (pnd 29 to 30) (g/kg/day)[d]			
#	136.1 ± 2.9 N=12	133.9 ± 4.1 N=13	143.3 ± 6.6 N=12
Feed Consumption (pnd 30 to 31) (g/kg/day)[d]			
	134.4 **‡** ± 4.8 **§** N=12	137.5 ± 3.1 N=13	151.2 * ± 6.0 N=12
Feed Consumption (pnd 31 to 32) (g/kg/day)[d]			
	135.7 ± 3.5 **§** N=12	141.3 ± 4.1 N=13	147.8 ± 3.6 N=12

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 6 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Feed Consumption (pnd 32 to 33) (g/kg/day)[d]			
	130.2 ± 2.9 N=12	126.3 ± 2.6 N=13	128.5 ± 4.8 N=11[f]
Feed Consumption (pnd 33 to 34) (g/kg/day)[d]			
	132.0 ± 3.3 N=12	123.4 ± 3.2 N=13	129.1 ± 2.8 N=12
Feed Consumption (pnd 34 to 35) (g/kg/day)[d]			
	133.0 ± 3.4 N=12	125.8 ± 3.7 N=13	129.0 ± 1.4 N=12
Feed Consumption (pnd 35 to 36) (g/kg/day)[d]			
	127.8 ‡‡ ± 4.0 N=12	143.6 ** ± 3.4 N=13	137.8 ± 2.4 N=12
Feed Consumption (pnd 36 to 37) (g/kg/day)[d]			
	126.6 ± 4.2 N=12	129.1 ± 2.7 N=13	131.2 ± 2.3 N=12
Feed Consumption (pnd 37 to 38) (g/kg/day)[d]			
	114.3 ± 2.2 § N=12	115.4 ± 1.9 N=13	121.7 ± 3.1 N=11[f]
Feed Consumption (pnd 38 to 39) (g/kg/day)[d]			
	113.9 ± 2.4 N=12	123.0 ± 3.2 N=13	121.6 ± 2.8 N=12
Feed Consumption (pnd 39 to 40) (g/kg/day)[d]			
	116.3 ‡ ± 2.6 § N=12	122.9 ± 1.9 N=13	125.1 * ± 2.3 N=12
Feed Consumption (pnd 40 to 41) (g/kg/day)[d]			
	115.4 ± 4.4 N=12	115.0 ± 3.0 N=13	117.6 ± 3.0 N=12

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 7 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Feed Consumption (pnd 41 to 42) (g/kg/day)[d]			
	106.7 ± 4.3 N=11[f]	112.4 ± 1.7 N=12[f]	114.1 ± 2.8 N=12
Feed Consumption (pnd 42 to 43) (g/kg/day)[d]			
	99.5 ± 3.9 § N=12	104.5 ± 4.7 N=13	111.9 ± 2.6 N=11[f]
Feed Consumption (pnd 43 to 44) (g/kg/day)[d]			
	105.6 ± 5.0 N=12	106.2 ± 2.0 N=13	107.0 ± 3.0 N=11[f]
Feed Consumption (pnd 44 to 45) (g/kg/day)[d]			
	97.5 ± 2.6 N=12	98.4 ± 2.8 N=13	101.5 ± 2.1 N=12
Feed Consumption (pnd 45 to 46) (g/kg/day)[d]			
	100.2 ± 2.4 § N=11[g]	91.8 ± 6.7 N=11[g]	85.5 ± 3.2 N=10[g]
Feed Consumption (pnd 46 to 47) (g/kg/day)[d]			
	94.7 ± 2.3 N=12	88.6 ± 4.4 N=13	91.3 ± 1.4 N=12
Feed Consumption (pnd 47 to 48) (g/kg/day)[d]			
	77.3 ‡‡‡ ± 3.1 §§ N=12	91.1 ** ± 2.5 N=13	91.9 ** ± 2.8 N=12
Feed Consumption (pnd 48 to 49) (g/kg/day)[d]			
	87.1 ± 1.9 N=12	88.1 ± 2.3 N=13	90.3 ± 1.7 N=12
Feed Consumption (pnd 49 to 50) (g/kg/day)[d]			
	87.8 ± 2.3 N=12	93.8 ± 3.4 N=13	90.5 ± 1.5 N=12

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 8 of 9)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Feed Consumption (pnd 50 to 51) (g/kg/day)[d]			
	92.7 ± 2.6 N=12	101.8 ± 3.5 N=13	97.1 ± 2.6 N=12
Feed Consumption (pnd 51 to 52) (g/kg/day)[d]			
	77.1 ‡‡ ± 2.0 § N=12	87.1 ** ± 2.1 N=13	86.8 * ± 2.7 N=12
Feed Consumption (pnd 52 to 53) (g/kg/day)[d,h]			
	76.4 ± 1.5 N=5	77.8 ± 3.8 N=5	72.4 ± 3.0 N=5
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[d]			
	108.3 ± 1.1 N=10[i]	110.4 ± 2.1 N=9[i]	112.4 ± 1.1 N=7[i]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[d,h]			
	104.5 ‡ ± 0.8 § N=4[i]	108.5 ± 1.5 N=3[i]	109.4 * ± 1.4 N=3[i]

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Vinclozolin Treated F_1 Males (page 9 of 9)

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[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 79 and 115 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Males 24, 114 and 131 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Reported as the mean $\pm$ S.E.M.; pnd = postnatal day.
[e]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[f]Decrease in N is due to the feed consumption value for one animal being a statistical outlier and therefore it was excluded.
[g]Decrease in N is due to one or more feed weights inadvertently not being recorded.
[h]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[i]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[‡]$p<0.05$; ANOVA Test.
[‡‡]$p<0.01$; ANOVA Test.
[‡‡‡]$p<0.001$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[§§]$p<0.01$; Test for Linear Trend.
[§§§]$p<0.001$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.
[**]$p<0.01$; Dunnett's Test.
[***]$p<0.001$; Dunnett's Test.
[††]$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
[Þ]$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model.
[ÞÞ]$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 1 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Males on Study	12[a]	15	13[b]
Feed Consumption (pnd 21 to 22) (g/day)[c]			
#	8.0 †† ± 0.5 ŸŸŸ N=11[d]	9.0 ± 0.3 N=15	12.0 ÞÞ ± 1.1 N=13
Feed Consumption (pnd 22 to 23) (g/day)[c]			
#	10.0 ± 0.5 Ÿ N=12	9.1 ± 0.3 N=15	7.4 ± 1.1 N=12[d]
Feed Consumption (pnd 23 to 24) (g/day)[c]			
	10.7 ± 0.5 N=12	11.0 ± 0.5 N=15	10.2 ± 0.8 N=13
Feed Consumption (pnd 24 to 25) (g/day)[c]			
	11.5 ± 0.4 N=12	11.8 ± 0.2 N=15	11.9 ± 0.4 N=12[e]
Feed Consumption (pnd 25 to 26) (g/day)[c]			
	11.8 ± 0.4 § N=12	12.3 ± 0.5 N=14[e]	13.3 ± 0.5 N=13
Feed Consumption (pnd 26 to 27) (g/day)[c]			
	13.6 ± 0.5 N=12	13.7 ± 0.3 N=15	13.2 ± 0.5 N=13
Feed Consumption (pnd 27 to 28) (g/day)[c]			
#	14.7 ± 0.9 N=12	13.6 ± 0.4 N=14[e]	14.1 ± 0.4 N=13
Feed Consumption (pnd 28 to 29) (g/day)[c]			
	13.1 ± 0.8 N=12	14.5 ± 0.3 N=15	14.6 ± 0.5 N=13
Feed Consumption (pnd 29 to 30) (g/day)[c]			
	15.2 ± 0.6 N=12	15.4 ± 0.4 N=14[e]	15.4 ± 0.5 N=13

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 2 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 30 to 31) (g/day)[c]			
	16.1 ± 0.7 N=12	15.6 ± 0.6 N=15	15.8 ± 0.5 N=13
Feed Consumption (pnd 31 to 32) (g/day)[c]			
	17.4 ± 0.6 N=12	16.5 ± 0.8 N=14[e]	17.4 ± 0.7 N=13
Feed Consumption (pnd 32 to 33) (g/day)[c]			
	17.9 ± 0.5 N=12	17.7 ± 1.0 N=15	18.8 ± 0.8 N=13
Feed Consumption (pnd 33 to 34) (g/day)[c]			
	19.4 ± 0.8 N=12	18.4 ± 1.3 N=14[f]	19.5 ± 0.9 N=13
Feed Consumption (pnd 34 to 35) (g/day)[c]			
#	20.8 ± 0.7 N=12	19.9 ± 1.1 N=15	23.5 ± 2.3 N=13
Feed Consumption (pnd 35 to 36) (g/day)[c]			
#	21.2 ± 0.7 N=12	22.0 ± 0.7 N=15	20.4 ± 1.9 N=13
Feed Consumption (pnd 36 to 37) (g/day)[c]			
	22.2 ± 0.5 N=12	21.5 ± 0.6 N=15	22.1 ± 0.7 N=13
Feed Consumption (pnd 37 to 38) (g/day)[c]			
	21.3 ± 0.7 N=12	21.4 ± 0.7 N=15	22.0 ± 0.9 N=13
Feed Consumption (pnd 38 to 39) (g/day)[c]			
	22.2 ± 0.7 N=12	21.8 ± 0.9 N=15	21.7 ± 0.8 N=13

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 3 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 39 to 40) (g/day)[c]	23.6 ± 0.6 N=12	22.9 ± 0.7 N=15	24.1 ± 1.0 N=13
Feed Consumption (pnd 40 to 41) (g/day)[c]	24.6 ± 1.3 N=12	22.9 ± 0.5 N=14[d]	23.1 ± 1.0 N=13
Feed Consumption (pnd 41 to 42) (g/day)[c]	23.2 ± 0.8 N=11[e]	24.6 ± 0.8 N=15	24.2 ± 0.7 N=12[e]
Feed Consumption (pnd 42 to 43) (g/day)[c]	23.0 ± 1.0 N=12	21.7 ± 0.6 N=15	23.3 ± 0.9 N=13
Feed Consumption (pnd 43 to 44) (g/day)[c]	25.3 ‡ ± 0.9 §§ N=12	23.1 ± 0.7 N=15	22.0 * ± 0.6 N=13
Feed Consumption (pnd 44 to 45) (g/day)[c]	24.3 ± 0.6 N=12	23.1 ± 0.6 N=15	23.4 ± 0.7 N=12[e]
Feed Consumption (pnd 45 to 46) (g/day)[c]	26.1 ‡ ± 0.7 N=11[g]	23.1 * ± 1.0 N=15	24.1 ± 0.7 N=11[g]
Feed Consumption (pnd 46 to 47) (g/day)[c]	25.2 ± 0.7 N=12	24.5 ± 0.8 N=15	24.8 ± 0.7 N=13
Feed Consumption (pnd 47 to 48) (g/day)[c]	21.2 ‡ ± 0.6 §§ N=12	23.3 ± 0.7 N=15	24.0 * ± 0.8 N=13

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 4 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 48 to 49) (g/day)[c]			
	24.7 ± 0.7 N=12	24.1 ± 0.9 N=15	23.5 ± 0.9 N=13
Feed Consumption (pnd 49 to 50) (g/day)[c]			
#	25.7 ± 0.6 N=12	24.5 ± 0.5 N=15	25.2 ± 0.9 N=13
Feed Consumption (pnd 50 to 51) (g/day)[c]			
	28.0 ± 0.9 N=12	26.7 ± 0.9 N=15	25.7 ± 0.8 N=13
Feed Consumption (pnd 51 to 52) (g/day)[c]			
	23.8 ± 0.6 § N=12	22.4 ± 0.8 N=15	21.6 ± 0.5 N=13
Feed Consumption (pnd 52 to 53) (g/day)[c,h]			
	25.2 ± 0.8 N=5	25.0 ± 1.3 N=7	26.8 ± 1.3 N=6
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[c]			
	20.2 ± 0.4 N=10[i]	19.7 ± 0.5 N=13[i]	20.8 ± 0.3 N=9[i]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[c,h]			
	20.7 ± 0.8 N=4[i]	19.8 ± 0.4 N=5[i]	21.2 ± 0.5 N=5[i]
Feed Consumption (pnd 21 to 22) (g/kg/day)[c]			
	137.4 ‡‡ ± 6.1 §§ N=11[d]	156.8 ± 8.4 N=15	210.4 ** ± 22.6 N=13
Feed Consumption (pnd 22 to 23) (g/kg/day)[c]			
#	158.3 † ± 7.2 Ÿ N=12	143.5 ± 3.1 N=15	118.0 Þ ± 18.2 N=12[d]

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 5 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 23 to 24) (g/kg/day)[c]			
	153.0 ± 4.3 N=12	156.9 ± 5.0 N=15	146.5 ± 8.7 N=13
Feed Consumption (pnd 24 to 25) (g/kg/day)[c]			
	150.4 ± 3.4 N=12	156.9 ± 7.3 N=15	159.6 ± 3.5 N=12[e]
Feed Consumption (pnd 25 to 26) (g/kg/day)[c]			
	143.8 ‡ ± 4.6 §§ N=12	147.6 ± 4.1 N=14[e]	160.9 * ± 3.6 N=13
Feed Consumption (pnd 26 to 27) (g/kg/day)[c]			
	153.6 ± 5.8 N=12	151.9 ± 3.0 N=15	148.4 ± 5.0 N=13
Feed Consumption (pnd 27 to 28) (g/kg/day)[c]			
	154.2 ± 11.8 N=12	140.2 ± 2.3 N=14[e]	145.5 ± 2.2 N=13
Feed Consumption (pnd 28 to 29) (g/kg/day)[c]			
	125.8 ‡ ± 6.1 § N=12	138.2 * ± 2.9 N=15	139.5 * ± 1.7 N=13
Feed Consumption (pnd 29 to 30) (g/kg/day)[c]			
	136.1 ± 2.9 N=12	136.4 ± 2.2 N=14[e]	137.7 ± 2.1 N=13
Feed Consumption (pnd 30 to 31) (g/kg/day)[c]			
	134.4 ± 4.8 N=12	129.3 ± 3.9 N=15	132.4 ± 2.5 N=13
Feed Consumption (pnd 31 to 32) (g/kg/day)[c]			
	135.7 ± 3.5 N=12	128.5 ± 5.2 N=14[e]	135.5 ± 2.8 N=13

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 6 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 32 to 33) (g/kg/day)[c]			
	130.2 ± 2.9 N=12	129.4 ± 6.4 N=15	136.4 ± 3.8 N=13
Feed Consumption (pnd 33 to 34) (g/kg/day)[c]			
#	132.0 ± 3.3 N=12	127.9 ± 9.4 N=14[f]	132.6 ± 3.6 N=13
Feed Consumption (pnd 34 to 35) (g/kg/day)[c]			
#	133.0 ± 3.4 N=12	129.6 ± 4.5 N=15	149.4 ± 12.4 N=13
Feed Consumption (pnd 35 to 36) (g/kg/day)[c]			
#	127.8 ± 4.0 N=12	135.2 ± 3.2 N=15	124.5 ± 11.5 N=13
Feed Consumption (pnd 36 to 37) (g/kg/day)[c]			
	126.6 ± 4.2 N=12	124.6 ± 4.3 N=15	126.2 ± 3.8 N=13
Feed Consumption (pnd 37 to 38) (g/kg/day)[c]			
	114.3 ± 2.2 N=12	116.9 ± 2.3 N=15	118.8 ± 3.9 N=13
Feed Consumption (pnd 38 to 39) (g/kg/day)[c]			
	113.9 ± 2.4 N=12	113.9 ± 4.3 N=15	112.2 ± 2.6 N=13
Feed Consumption (pnd 39 to 40) (g/kg/day)[c]			
	116.3 ± 2.6 N=12	114.8 ± 2.6 N=15	119.2 ± 3.5 N=13
Feed Consumption (pnd 40 to 41) (g/kg/day)[c]			
	115.4 ± 4.4 N=12	110.5 ± 2.1 N=13[d,j]	109.8 ± 2.9 N=13

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 7 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 41 to 42) (g/kg/day)[c]			
	106.7 ± 4.3 N=11[e]	112.4 ± 3.0 N=14	111.3 ± 3.1 N=12[e]
Feed Consumption (pnd 42 to 43) (g/kg/day)[c]			
	99.5 ± 3.9 N=12	96.1 ± 1.8 N=15	103.1 ± 3.1 N=13
Feed Consumption (pnd 43 to 44) (g/kg/day)[c]			
	105.6 ± 5.0 § N=12	98.7 ± 1.9 N=15	94.5 ± 2.2 N=13
Feed Consumption (pnd 44 to 45) (g/kg/day)[c]			
	97.5 ± 2.6 N=12	95.4 ± 1.8 N=15	96.8 ± 2.7 N=12[e]
Feed Consumption (pnd 45 to 46) (g/kg/day)[c]			
	100.2 ± 2.4 N=11[g]	92.5 ± 4.8 N=15	92.8 ± 2.4 N=11[g]
Feed Consumption (pnd 46 to 47) (g/kg/day)[c]			
	94.7 ± 2.3 N=12	95.1 ± 3.4 N=15	96.3 ± 2.5 N=13
Feed Consumption (pnd 47 to 48) (g/kg/day)[c]			
	77.3 ‡‡ ± 3.1 §§§ N=12	87.1 * ± 1.8 N=15	89.9 ** ± 2.3 N=13
Feed Consumption (pnd 48 to 49) (g/kg/day)[c]			
	87.1 ± 1.9 N=12	87.3 ± 2.2 N=15	85.1 ± 1.7 N=13
Feed Consumption (pnd 49 to 50) (g/kg/day)[c]			
	87.8 ± 2.3 N=12	86.2 ± 1.4 N=15	88.6 ± 2.4 N=13

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 8 of 9)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 50 to 51) (g/kg/day)[c]			
	92.7 ± 2.6 N=12	91.9 ± 3.0 N=15	89.1 ± 1.8 N=13
Feed Consumption (pnd 51 to 52) (g/kg/day)[c]			
	77.1 ± 2.0 N=12	75.5 ± 2.9 N=15	73.9 ± 2.0 N=13
Feed Consumption (pnd 52 to 53) (g/kg/day)[c,h]			
	76.4 ± 1.5 N=5	79.8 ± 3.3 N=7	83.4 ± 4.5 N=6
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[c]			
	108.3 ± 1.1 N=10[i]	109.1 ± 2.0 N=12[i]	109.7 ± 1.2 N=9[i]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[c,h]			
	104.5 ± 0.8 N=4[i]	103.1 ± 1.9 N=5[i]	107.1 ± 1.8 N=5[i]

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor Treated F_1 Males (page 9 of 9)

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 17 and 30 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Reported as the mean ± S.E.M.; pnd = postnatal day.
[d]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[e]Decrease in N is due to the feed consumption value for one animal being a statistical outlier and therefore it was excluded.
[f]Decrease in N is due to one animal pulling the feed out of the feed hopper and into the cage and therefore an accurate feed weight could not be obtained.
[g]Decrease in N is due to one or more feed weights inadvertently not being recorded.
[h]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[i]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[j]Decrease in N is due to one body weight on postnatal day 41 inadvertently not being recorded.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[†]$p<0.05$; Wald Chi-square Test for overall treatment effect in robust regression model.
[††]$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
[Ÿ]$p<0.05$; Linear trend test in robust regression model.
[ŸŸ]$p<0.01$; Linear trend test in robust regression model.
[Þ]$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model.
[ÞÞ]$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
[‡]$p<0.05$; ANOVA Test.
[‡‡]$p<0.01$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[§§]$p<0.01$; Test for Linear Trend.
[§§§]$p<0.001$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.
[**]$p<0.01$; Dunnett's Test.

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 1 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Males on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	5.7 ± 0.4 N=15	6.4 ± 0.5 N=15	7.1 ± 0.4 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	10.1 ± 0.3 N=15	9.8 ± 0.3 N=15	10.0 ± 0.3 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	10.3 ± 0.2 N=13[b]	10.7 ± 0.2 N=15	10.3 ± 0.2 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	12.1 ± 0.4 N=14[b]	12.4 ± 0.4 N=15	11.5 ± 0.3 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	11.8 ‡ ± 0.3 N=15	13.0 ** ± 0.4 N=15	12.1 ± 0.3 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	12.8 ± 0.3 N=15	12.9 ± 0.4 N=15	13.3 ± 0.3 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
#	15.0 ± 0.8 N=15	15.6 ± 0.4 N=15	15.1 ± 0.4 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	14.1 ± 0.3 N=15	14.4 ± 0.5 N=15	13.7 ± 0.4 N=15
Feed Consumption (pnd 29 to 30) (g/day)[a]			
	14.4 ± 0.5 N=15	14.9 ± 0.5 N=15	13.5 ± 0.5 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 2 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 30 to 31) (g/day)[a]			
	15.6 ‡‡ ± 0.5 §§ N=14[c]	16.3 ± 0.3 N=15	14.3 ± 0.5 N=14[b]
Feed Consumption (pnd 31 to 32) (g/day)[a]			
	17.5 ‡‡‡ ± 0.6 §§§ N=14	18.0 ± 0.3 N=15	14.6 *** ± 0.5 N=14[b]
Feed Consumption (pnd 32 to 33) (g/day)[a]			
	18.5 ‡‡‡ ± 0.8 §§§ N=14	18.2 ± 0.4 N=15	14.6 *** ± 0.6 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]			
	18.5 ‡‡‡ ± 0.4 §§§ N=14	18.9 ± 0.5 N=15	13.9 *** ± 0.8 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]			
	19.6 ‡‡‡ ± 1.1 §§§ N=14	20.6 ± 0.4 N=14[b]	15.0 *** ± 0.9 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]			
	20.4 ‡‡‡ ± 0.8 §§§ N=14	21.3 ± 0.7 N=15	13.9 *** ± 0.5 N=15
Feed Consumption (pnd 36 to 37) (g/day)[a]			
	21.9 ‡‡‡ ± 0.4 §§§ N=14	22.4 ± 0.6 N=15	13.6 *** ± 0.5 N=15
Feed Consumption (pnd 37 to 38) (g/day)[a]			
	22.3 ‡‡‡ ± 0.6 §§§ N=14	22.4 ± 0.6 N=15	15.4 *** ± 1.0 N=15
Feed Consumption (pnd 38 to 39) (g/day)[a]			
#	22.8 ††† ± 0.6 ŸŸŸ N=14	22.6 ± 0.4 N=15	12.7 ÞÞÞ ± 1.0 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 3 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 39 to 40) (g/day)[a]			
	22.9 ‡‡‡ ± 0.5 §§§ N=14	23.4 ± 0.5 N=15	13.1 *** ± 0.5 N=15
Feed Consumption (pnd 40 to 41) (g/day)[a]			
	22.8 ‡‡‡ ± 0.5 §§§ N=14	22.6 ± 0.5 N=15	11.5 *** ± 0.4 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a]			
	24.3 ‡‡‡ ± 0.7 §§§ N=14	23.4 ± 0.7 N=15	12.8 *** ± 0.5 N=15
Feed Consumption (pnd 42 to 43) (g/day)[a]			
	23.3 ‡‡‡ ± 0.8 §§§ N=14	24.0 ± 0.7 N=15	12.3 *** ± 0.4 N=15
Feed Consumption (pnd 43 to 44) (g/day)[a]			
	23.1 ‡‡‡ ± 0.8 §§§ N=14	22.7 ± 0.7 N=15	11.1 *** ± 0.3 N=15
Feed Consumption (pnd 44 to 45) (g/day)[a]			
	23.6 ‡‡‡ ± 0.5 §§§ N=14	22.0 ± 0.7 N=15	11.4 *** ± 0.5 N=14[b]
Feed Consumption (pnd 45 to 46) (g/day)[a]			
	25.0 ‡‡‡ ± 0.8 §§§ N=14	22.7 * ± 0.6 N=15	11.2 *** ± 0.2 N=14[d]
Feed Consumption (pnd 46 to 47) (g/day)[a]			
	24.9 ‡‡‡ ± 0.5 §§§ N=13[b]	22.0 *** ± 0.6 N=15	11.3 *** ± 0.3 N=15
Feed Consumption (pnd 47 to 48) (g/day)[a]			
	24.6 ‡‡‡ ± 0.5 §§§ N=13[b]	21.4 *** ± 0.7 N=15	11.0 *** ± 0.4 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 4 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 48 to 49) (g/day)[a]	25.2 ‡‡‡ ± 0.9 §§§ N=14	21.4 ** ± 1.0 N=15	11.0 *** ± 0.4 N=15
Feed Consumption (pnd 49 to 50) (g/day)[a]	25.8 ‡‡‡ ± 0.9 §§§ N=14	21.3 *** ± 0.7 N=15	10.9 *** ± 0.3 N=14[e]
Feed Consumption (pnd 50 to 51) (g/day)[a]	26.6 ‡‡‡ ± 0.8 §§§ N=14	21.9 *** ± 0.8 N=15	10.8 *** ± 0.4 N=14
Feed Consumption (pnd 51 to 52) (g/day)[a]	25.6 ‡‡‡ ± 0.7 §§§ N=14	19.3 *** ± 0.8 N=15	9.6 *** ± 0.2 N=14
Feed Consumption (pnd 52 to 53) (g/day)[a,f]	25.9 ‡‡‡ ± 1.0 §§§ N=5	18.4 *** ± 0.8 N=5	9.7 *** ± 0.4 N=4
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[a]	20.5 ‡‡‡ ± 0.4 §§§ N=12[g]	19.4 ± 0.4 N=14[g]	12.6 *** ± 0.3 N=12[g]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[a,f]	20.7 ‡‡‡ ± 0.4 §§§ N=5	19.6 ± 0.4 N=5	13.4 *** ± 0.1 N=3[g]
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	98.2 ± 7.0 N=15	110.5 ± 8.8 N=15	120.6 ± 6.0 N=15
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]	158.7 ± 3.9 N=15	153.7 ± 3.9 N=15	157.1 ± 3.0 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 5 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
	144.5 ± 2.4 N=13[b]	152.6 ± 2.5 N=15	149.1 ± 3.1 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	154.9 ± 4.8 N=14[b]	159.1 ± 3.4 N=15	151.0 ± 3.0 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	141.4 ± 3.2 N=15	152.9 ± 3.8 N=15	145.2 ± 2.8 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	142.6 ± 2.4 N=15	141.0 ± 4.6 N=15	147.8 ± 2.7 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	153.1 ± 5.8 N=15	156.3 ± 3.1 N=15	155.0 ± 2.7 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	134.9 ± 3.5 N=15	134.3 ± 5.6 N=15	131.6 ± 4.6 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
	127.3 ± 2.4 **§** N=15	128.8 ± 2.3 N=15	120.3 ± 3.4 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	128.9 **‡‡** ± 2.4 **§§** N=14[c]	132.2 ± 2.1 N=15	120.6 ***** ± 2.7 N=14[b]
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]			
	134.2 **‡‡‡** ± 2.3 **§§§** N=14	135.7 ± 2.4 N=15	114.5 ******* ± 2.5 N=14[b]

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 6 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	132.2 ‡‡ ± 3.9 §§§ N=14	128.1 ± 2.2 N=15	111.3 ** ± 5.1 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	124.3 ‡‡‡ ± 2.6 §§§ N=14	124.8 ± 2.6 N=15	101.6 *** ± 4.5 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	123.7 ± 5.6 § N=14	128.3 ± 2.3 N=14[b]	107.5 ± 8.7 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	121.9 ‡‡‡ ± 2.8 §§§ N=14	124.6 ± 3.6 N=15	94.4 *** ± 1.4 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	123.5 ‡‡‡ ± 1.7 §§§ N=14	123.9 ± 2.4 N=15	89.8 *** ± 1.7 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
#	118.7 †† ± 1.7 ŸŸŸ N=14	117.3 ± 2.2 N=15	98.6 ÞÞÞ ± 5.3 N=15
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
#	115.9 ††† ± 3.0 ŸŸŸ N=14	112.6 ± 1.6 N=15	80.4 ÞÞÞ ± 6.4 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
	111.3 ‡‡‡ ± 1.9 §§§ N=14	111.2 ± 1.7 N=15	81.0 *** ± 1.6 N=15
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
	106.5 ‡‡‡ ± 2.0 §§§ N=14	103.1 ± 1.4 N=15	70.5 *** ± 1.7 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 7 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
	108.8 ‡‡‡ ± 2.5 §§§ N=14	103.2 ± 2.2 N=15	78.0 *** ± 1.5 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[a]			
	100.4 ‡‡‡ ± 3.0 §§§ N=14	102.3 ± 2.2 N=15	74.2 *** ± 1.7 N=15
Feed Consumption (pnd 43 to 44) (g/kg/day)[a]			
	95.9 ‡‡‡ ± 2.4 §§§ N=14	93.6 ± 2.2 N=15	67.1 *** ± 1.5 N=15
Feed Consumption (pnd 44 to 45) (g/kg/day)[a]			
	94.7 ‡‡‡ ± 1.2 §§§ N=14	87.5 ** ± 1.7 N=15	68.0 *** ± 1.7 N=14[b]
Feed Consumption (pnd 45 to 46) (g/kg/day)[a]			
	96.2 ‡‡‡ ± 1.8 §§§ N=14	87.7 ** ± 1.4 N=15	67.1 *** ± 1.8 N=14[d]
Feed Consumption (pnd 46 to 47) (g/kg/day)[a]			
	91.6 ‡‡‡ ± 2.0 §§§ N=13[b]	82.8 ** ± 1.8 N=15	66.9 *** ± 1.4 N=15
Feed Consumption (pnd 47 to 48) (g/kg/day)[a]			
	87.3 ‡‡‡ ± 1.2 §§§ N=13[b]	78.5 ** ± 2.0 N=15	65.1 *** ± 2.5 N=15
Feed Consumption (pnd 48 to 49) (g/kg/day)[a]			
	87.6 ‡‡‡ ± 2.2 §§§ N=14	76.7 ** ± 2.4 N=15	64.5 *** ± 1.7 N=15
Feed Consumption (pnd 49 to 50) (g/kg/day)[a]			
	86.7 ‡‡‡ ± 1.9 §§§ N=14	74.9 *** ± 1.7 N=15	64.3 *** ± 1.4 N=14[e]

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 8 of 9)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 50 to 51) (g/kg/day)[a]			
	86.7 ‡‡‡ ± 1.5 §§§ N=14	75.5 *** ± 1.5 N=15	63.3 *** ± 1.8 N=14
Feed Consumption (pnd 51 to 52) (g/kg/day)[a]			
	81.0 ‡‡‡ ± 1.3 §§§ N=14	65.0 *** ± 1.5 N=15	56.0 *** ± 1.7 N=14
Feed Consumption (pnd 52 to 53) (g/kg/day)[a,f]			
	78.1 ‡‡‡ ± 1.5 §§ N=5	61.0 *** ± 2.2 N=5	52.4 *** ± 1.8 N=4
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[a]			
	107.3 ‡‡‡ ± 0.9 §§§ N=12[g]	103.6 * ± 0.9 N=14[g]	89.6 *** ± 1.0 N=12[g]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[a,f]			
	103.7 ‡‡‡ ± 1.1 §§§ N=5	99.8 ± 1.4 N=5	89.1 *** ± 1.5 N=3[g]

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil Treated F_1 Males (page 9 of 9)

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[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrease in N is due to the feed consumption value for one or more animals being a statistical outlier and therefore it was excluded.
[c]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[d]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[e]Male 268 was found dead on postnatal day 50 prior to dosing.
[f]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[g]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[‡]$p<0.05$; ANOVA Test.
[‡‡]$p<0.01$; ANOVA Test.
[‡‡‡]$p<0.001$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[§§]$p<0.01$; Test for Linear Trend.
[§§§]$p<0.001$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.
[**]$p<0.01$; Dunnett's Test.
[***]$p<0.001$; Dunnett's Test.
[††]$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
[†††]$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
[ŸŸŸ]$p<0.001$; Linear trend test in robust regression model.
[ÞÞÞ]$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 1 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	5.7 ‡‡‡ ± 0.4 § N=15	9.3 *** ± 0.8 N=14[b]	8.0 * ± 0.5 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	10.1 ± 0.3 N=15	9.3 ± 0.9 N=14[c]	10.4 ± 0.5 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	10.3 ‡ ± 0.2 N=13[b]	11.2 * ± 0.3 N=15	10.9 ± 0.3 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	12.1 ± 0.4 N=14[b]	12.1 ± 0.3 N=15	11.4 ± 0.3 N=14[b]
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	11.8 ± 0.3 N=15	11.9 ± 0.2 N=15	11.9 ± 0.3 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	12.8 ± 0.3 N=15	13.8 ± 0.5 N=15	12.6 ± 0.6 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
	15.0 ± 0.8 N=15	15.6 ± 0.6 N=15	15.7 ± 0.5 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	14.1 ± 0.3 N=15	14.8 ± 0.6 N=15	14.3 ± 0.4 N=14[b]
Feed Consumption (pnd 29 to 30) (g/day)[a]			
	14.4 ± 0.5 N=15	15.0 ± 0.5 N=15	14.0 ± 0.9 N=15

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 2 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 30 to 31) (g/day)[a]			
	15.6 ± 0.5 N=14[d]	16.1 ± 0.5 N=15	15.9 ± 0.6 N=14[b]
Feed Consumption (pnd 31 to 32) (g/day)[a]			
	17.5 ± 0.6 N=14	17.3 ± 0.4 N=15	16.4 ± 0.5 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]			
	18.5 ± 0.8 N=14	18.9 ± 0.5 N=15	17.8 ± 0.7 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]			
	18.5 ± 0.4 N=14	19.3 ± 0.4 N=15	18.2 ± 0.6 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]			
	19.6 ± 1.1 N=14	20.0 ± 1.0 N=15	20.6 ± 0.6 N=14[c]
Feed Consumption (pnd 35 to 36) (g/day)[a]			
	20.4 ± 0.8 N=14	21.2 ± 0.5 N=15	20.3 ± 0.6 N=14[b]
Feed Consumption (pnd 36 to 37) (g/day)[a]			
	21.9 ‡ ± 0.4 N=14	24.0 * ± 0.7 N=15	21.9 ± 0.7 N=14[e]
Feed Consumption (pnd 37 to 38) (g/day)[a]			
#	22.3 ± 0.6 N=14	23.5 ± 1.0 N=15	22.4 ± 0.5 N=14
Feed Consumption (pnd 38 to 39) (g/day)[a]			
	22.8 ± 0.6 N=14	22.5 ± 0.9 N=15	23.1 ± 0.8 N=14

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 3 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 39 to 40) (g/day)[a]			
	22.9 ± 0.5 N=14	23.7 ± 0.7 N=15	22.2 ± 0.6 N=14
Feed Consumption (pnd 40 to 41) (g/day)[a]			
#	22.8 ± 0.5 N=14	23.8 ± 0.4 N=14[b]	22.6 ± 1.2 N=13[b]
Feed Consumption (pnd 41 to 42) (g/day)[a]			
	24.3 ± 0.7 N=14	24.6 ± 0.8 N=15	25.3 ± 0.7 N=13[b]
Feed Consumption (pnd 42 to 43) (g/day)[a]			
	23.3 ± 0.8 N=14	25.3 ± 0.6 N=15	23.9 ± 1.1 N=14
Feed Consumption (pnd 43 to 44) (g/day)[a]			
	23.1 ± 0.8 N=14	24.3 ± 0.8 N=15	24.4 ± 0.7 N=14
Feed Consumption (pnd 44 to 45) (g/day)[a]			
	23.6 ± 0.5 N=14	24.3 ± 0.4 N=15	22.8 ± 0.6 N=14
Feed Consumption (pnd 45 to 46) (g/day)[a]			
	25.0 ± 0.8 N=14	24.2 ± 0.7 N=15	24.1 ± 0.9 N=14
Feed Consumption (pnd 46 to 47) (g/day)[a]			
	24.9 ± 0.5 N=13[b]	26.3 ± 0.8 N=15	25.5 ± 0.8 N=14
Feed Consumption (pnd 47 to 48) (g/day)[a]			
	24.6 ± 0.5 N=13[b]	25.3 ± 0.6 N=15	23.2 ± 0.7 N=14

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 4 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 48 to 49) (g/day)[a]	25.2 ± 0.9 N=14	25.7 ± 0.5 N=15	24.7 ± 1.0 N=14
Feed Consumption (pnd 49 to 50) (g/day)[a]	25.8 ± 0.9 N=14	26.4 ± 0.8 N=15	26.3 ± 0.7 N=14
Feed Consumption (pnd 50 to 51) (g/day)[a]	26.6 ± 0.8 N=14	27.4 ± 0.6 N=15	26.9 ± 0.8 N=14
Feed Consumption (pnd 51 to 52) (g/day)[a]	25.6 ± 0.7 N=14	26.2 ± 0.6 N=14[b]	24.1 ± 0.9 N=14
Feed Consumption (pnd 52 to 53) (g/day)[a,f]	25.9 ± 1.0 N=5	27.2 ± 0.5 N=5	28.4 ± 1.2 N=4
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[a]	20.5 ± 0.4 N=12[g]	21.0 ± 0.4 N=13[g]	19.7 ± 0.6 N=9[g]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[a,f]	20.7 ± 0.4 § N=5	21.8 ± 0.6 N=5	22.7 ± 0.3 N=2[g]
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	98.2 ‡‡ ± 7.0 § N=15	162.7 *** ± 17.4 N=14[b]	139.0 * ± 8.7 N=15
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]	158.7 ± 3.9 N=15	144.4 ± 12.0 N=14[c]	164.6 ± 5.1 N=15

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 5 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
#	144.5 ††† ± 2.4 ŸŸ N=13[b]	162.2 ÞÞ ± 4.5 N=15	157.8 ÞÞÞ ± 2.9 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]	154.9 ± 4.8 N=14[b]	158.5 ± 2.7 N=15	154.2 ± 3.8 N=14[b]
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]	141.4 ± 3.2 N=15	144.6 ± 2.6 N=15	147.7 ± 2.8 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]	142.6 ± 2.4 N=15	154.5 ± 3.1 N=15	144.0 ± 5.0 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]	153.1 ± 5.8 N=15	160.1 ± 4.6 N=15	165.9 ± 2.9 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]	134.9 ± 3.5 N=15	141.9 ± 5.7 N=15	141.1 ± 5.0 N=14[b]
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]	127.3 ± 2.4 N=15	133.1 ± 2.3 N=15	127.5 ± 6.9 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]	128.9 ± 2.4 N=14[d]	133.0 ± 2.3 N=15	136.0 ± 2.9 N=14[b]
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]	134.2 ± 2.3 N=14	133.6 ± 1.7 N=15	131.0 ± 3.3 N=15

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 6 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	132.2 ± 3.9 N=14	136.6 ± 2.1 N=15	132.6 ± 3.5 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	124.3 ± 2.6 N=14	131.7 ± 2.5 N=15	128.3 ± 4.2 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	123.7 ± 5.6 N=14	127.1 ± 4.6 N=15	136.1 ± 2.0 N=14[c]
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	121.9 ± 2.8 N=14	127.2 ± 1.7 N=15	126.5 ± 2.5 N=14[b]
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	123.5 ‡‡ ± 1.7 N=14	136.0 ** ± 3.2 N=15	128.7 ± 2.3 N=14[e]
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
	118.7 ± 1.7 N=14	125.5 ± 4.5 N=15	125.6 ± 2.3 N=14
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
	115.9 ± 3.0 N=14	115.0 ± 3.7 N=15	122.9 ± 3.4 N=14
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
	111.3 ± 1.9 N=14	116.9 ± 3.1 N=15	113.4 ± 2.6 N=14
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
#	106.5 ± 2.0 N=14	111.2 ± 2.0 N=14[b]	111.2 ± 4.7 N=13[b]

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 7 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]	108.8 ‡ ± 2.5 §§ N=14	111.9 ± 2.2 N=15	120.1 ** ± 3.0 N=13[b]
Feed Consumption (pnd 42 to 43) (g/kg/day)[a]	100.4 ± 3.0 N=14	110.9 ± 3.2 N=15	108.1 ± 4.5 N=14
Feed Consumption (pnd 43 to 44) (g/kg/day)[a]	95.9 ‡ ± 2.4 §§ N=14	102.0 ± 2.1 N=15	106.2 ** ± 2.2 N=14
Feed Consumption (pnd 44 to 45) (g/kg/day)[a]	94.7 ± 1.2 N=14	98.5 ± 2.0 N=15	96.4 ± 2.3 N=14
Feed Consumption (pnd 45 to 46) (g/kg/day)[a]	96.2 ± 1.8 N=14	94.7 ± 2.0 N=15	98.0 ± 2.5 N=14
Feed Consumption (pnd 46 to 47) (g/kg/day)[a]	91.6 ± 2.0 § N=13[b]	99.7 ± 3.9 N=15	100.3 ± 1.5 N=14
Feed Consumption (pnd 47 to 48) (g/kg/day)[a]	87.3 ± 1.2 N=13[b]	92.7 ± 2.6 N=15	88.8 ± 2.5 N=14
Feed Consumption (pnd 48 to 49) (g/kg/day)[a]	87.6 ± 2.2 N=14	90.9 ± 1.3 N=15	91.1 ± 2.0 N=14
Feed Consumption (pnd 49 to 50) (g/kg/day)[a]	86.7 ‡ ± 1.9 §§ N=14	89.9 ± 1.7 N=15	94.1 ** ± 1.2 N=14

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 8 of 9)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 50 to 51) (g/kg/day)[a]			
	86.7 ± 1.5 § N=14	90.7 ± 1.9 N=15	92.8 ± 1.7 N=14
Feed Consumption (pnd 51 to 52) (g/kg/day)[a]			
	81.0 ± 1.3 N=14	83.3 ± 1.3 N=14[b]	80.2 ± 2.0 N=14
Feed Consumption (pnd 52 to 53) (g/kg/day)[a,f]			
	78.1 ± 1.5 N=5	82.0 ± 2.8 N=5	83.8 ± 2.8 N=4
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[a]			
	107.3 ‡‡ ± 0.9 §§ N=12[g]	111.3 ** ± 0.7 N=13[g]	112.3 ** ± 1.3 N=9[g]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[a,f]			
	103.7 ‡‡ ± 1.1 §§§ N=5	110.1 ** ± 0.7 N=5	111.6 ** ± 2.0 N=2[g]

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole Treated F_1 Males (page 9 of 9)

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrease in N is due to the feed consumption value for one or more animals being a statistical outlier and therefore it was excluded.
[c]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[d]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[e]Male 242 was found dead on postnatal day 37 prior to dosing (misdirected dose).
[f]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[g]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡$p<0.05$; ANOVA Test.
‡‡$p<0.01$; ANOVA Test.
‡‡‡$p<0.001$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§$p<0.01$; Test for Linear Trend.
§§§$p<0.001$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.
**$p<0.01$; Dunnett's Test.
***$p<0.001$; Dunnett's Test.
†††$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸ$p<0.01$; Linear trend test in robust regression model.
ÞÞ$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
ÞÞÞ$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 1 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	5.7 ‡‡ ± 0.4 §§§ N=15	7.0 ± 0.5 N=15	8.5 ** ± 0.6 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	10.1 ± 0.3 N=15	10.1 ± 0.4 N=15	9.2 ± 0.6 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
#	10.3 †† ± 0.2 ŸŸ N=13[b]	9.6 ÞÞ ± 0.2 N=15	9.0 ÞÞ ± 0.5 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	12.1 ‡‡‡ ± 0.4 §§§ N=14[b]	10.3 ** ± 0.3 N=15	9.9 *** ± 0.4 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	11.8 ‡‡‡ ± 0.3 §§§ N=15	10.7 * ± 0.3 N=15	9.7 *** ± 0.3 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	12.8 ‡‡ ± 0.3 §§§ N=15	11.7 ± 0.3 N=15	10.9 ** ± 0.5 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
	15.0 ± 0.8 § N=15	13.5 ± 0.5 N=15	13.3 ± 0.5 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	14.1 ‡‡ ± 0.3 §§§ N=15	12.8 * ± 0.3 N=15	11.8 *** ± 0.5 N=15
Feed Consumption (pnd 29 to 30) (g/day)[a]			
	14.4 ‡ ± 0.5 §§ N=15	13.1 ± 0.3 N=15	12.6 ** ± 0.5 N=15

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 2 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 30 to 31) (g/day)[a]			
	15.6 ‡‡ ± 0.5 §§ N=14[c]	14.3 ± 0.4 N=15	13.2 ** ± 0.5 N=15
Feed Consumption (pnd 31 to 32) (g/day)[a]			
	17.5 ‡‡‡ ± 0.6 §§§ N=14	15.2 ** ± 0.4 N=15	13.8 *** ± 0.4 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]			
	18.5 ‡‡ ± 0.8 §§§ N=14	16.8 ± 0.6 N=15	15.2 ** ± 0.6 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]			
	18.5 ‡‡ ± 0.4 §§§ N=14	17.5 ± 0.9 N=15	15.3 ** ± 0.4 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]			
#	19.6 ± 1.1 N=14	18.5 ± 0.4 N=15	17.7 ± 0.4 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]			
	20.4 ± 0.8 N=14	19.3 ± 0.4 N=15	19.0 ± 0.8 N=15
Feed Consumption (pnd 36 to 37) (g/day)[a]			
	21.9 ‡ ± 0.4 §§ N=14	20.8 ± 0.5 N=15	19.3 * ± 0.8 N=15
Feed Consumption (pnd 37 to 38) (g/day)[a]			
	22.3 ± 0.6 N=14	20.4 ± 0.4 N=15	21.3 ± 1.0 N=15
Feed Consumption (pnd 38 to 39) (g/day)[a]			
#	22.8 ± 0.6 N=14	22.7 ± 0.7 N=15	20.8 ± 1.8 N=15

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 3 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 39 to 40) (g/day)[a]	22.9 ‡‡‡ ± 0.5 §§§ N=14	22.2 ± 0.5 N=15	18.8 *** ± 1.0 N=14[d]
Feed Consumption (pnd 40 to 41) (g/day)[a]	22.8 ‡‡ ± 0.5 §§ N=14	22.5 ± 0.4 N=15	20.1 ** ± 0.6 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a]	24.3 ± 0.7 N=14	23.3 ± 0.6 N=15	22.1 ± 1.2 N=15
Feed Consumption (pnd 42 to 43) (g/day)[a]	23.3 ‡ ± 0.8 § N=14	23.4 ± 0.5 N=15	21.2 ± 0.7 N=15
Feed Consumption (pnd 43 to 44) (g/day)[a]	23.1 ‡‡ ± 0.8 §§ N=14	23.5 ± 0.4 N=15	20.3 ** ± 0.7 N=15
Feed Consumption (pnd 44 to 45) (g/day)[a]	23.6 ‡ ± 0.5 § N=14	23.2 ± 0.9 N=15	21.2 * ± 0.5 N=14[d]
Feed Consumption (pnd 45 to 46) (g/day)[a]	25.0 ‡‡‡ ± 0.8 §§§ N=14	24.4 ± 0.5 N=14[b]	21.1 *** ± 0.6 N=14[b]
Feed Consumption (pnd 46 to 47) (g/day)[a]	24.9 ‡ ± 0.5 § N=13[b]	23.8 ± 0.5 N=15	22.8 * ± 0.6 N=15
Feed Consumption (pnd 47 to 48) (g/day)[a]	24.6 ‡‡ ± 0.5 §§ N=13[b]	24.8 ± 0.6 N=15	22.1 ** ± 0.6 N=15

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 4 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 48 to 49) (g/day)[a]	25.2 ‡‡ ± 0.9 §§ N=14	24.9 ± 0.5 N=15	21.7 ** ± 0.7 N=15
Feed Consumption (pnd 49 to 50) (g/day)[a]	25.8 ‡‡ ± 0.9 §§ N=14	25.1 ± 0.6 N=15	21.9 ** ± 0.9 N=15
Feed Consumption (pnd 50 to 51) (g/day)[a]	26.6 ‡‡ ± 0.8 §§§ N=14	25.6 ± 0.4 N=15	22.9 *** ± 0.8 N=15
Feed Consumption (pnd 51 to 52) (g/day)[a]	25.6 ‡‡ ± 0.7 §§ N=14	25.1 ± 0.7 N=15	21.6 ** ± 0.9 N=15
Feed Consumption (pnd 52 to 53) (g/day)[a,e]	25.9 ± 1.0 N=5	25.8 ± 0.9 N=5	23.2 ± 1.2 N=5
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[a]	20.5 ‡‡‡ ± 0.4 §§§ N=12[f]	19.3 ± 0.3 N=14[f]	17.7 *** ± 0.5 N=13[f]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[a,e]	20.7 ± 0.4 § N=5	20.2 ± 0.7 N=5	18.2 ± 0.8 N=5
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	98.2 ‡‡ ± 7.0 §§ N=15	120.1 ± 9.3 N=15	147.6 ** ± 13.9 N=15
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]	158.7 ± 3.9 N=15	159.5 ± 5.1 N=15	146.4 ± 8.1 N=15

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 5 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
#	144.5 ± 2.4 N=13[b]	139.1 ± 3.6 N=15	132.9 ± 5.8 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	154.9 ‡ ± 4.8 §§ N=14[b]	138.6 * ± 3.7 N=15	137.9 * ± 4.4 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	141.4 ‡ ± 3.2 §§ N=15	134.7 ± 3.7 N=15	126.7 ** ± 3.4 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	142.6 ± 2.4 § N=15	137.3 ± 2.5 N=15	132.7 ± 4.5 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	153.1 ± 5.8 N=15	145.5 ± 3.3 N=15	149.1 ± 3.6 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	134.9 ± 3.5 N=15	128.2 ± 4.0 N=15	124.4 ± 5.2 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
#	127.3 ± 2.4 N=15	122.3 ± 1.8 N=15	124.2 ± 4.5 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	128.9 ± 2.4 N=14[c]	125.7 ± 3.2 N=15	121.3 ± 3.4 N=15
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]			
	134.2 ‡‡‡ ± 2.3 §§§ N=14	124.8 ** ± 1.9 N=15	119.8 *** ± 2.1 N=15

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 6 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	132.2 ± 3.9 N=14	128.9 ± 3.1 N=15	123.4 ± 2.9 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	124.3 ± 2.6 N=14	126.4 ± 6.2 N=15	117.8 ± 2.1 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	123.7 ± 5.6 N=14	126.0 ± 2.5 N=15	128.7 ± 1.9 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	121.9 ± 2.8 N=14	123.3 ± 2.1 N=15	128.3 ± 3.4 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	123.5 ± 1.7 N=14	125.4 ± 1.8 N=15	123.1 ± 4.1 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
#	118.7 ± 1.7 N=14	116.8 ± 2.2 N=15	129.1 ± 5.2 N=15
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
	115.9 ± 3.0 N=14	123.5 ± 3.5 N=15	121.8 ± 11.7 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
	111.3 ± 1.9 N=14	115.3 ± 2.9 N=15	103.4 ± 5.0 N=14[d]
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
	106.5 ± 2.0 N=14	111.7 ± 1.8 N=15	107.7 ± 2.8 N=15

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 7 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
	108.8 ± 2.5 N=14	111.2 ± 2.6 N=15	112.5 ± 4.0 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[a]			
	100.4 ± 3.0 N=14	107.8 ± 2.5 N=15	105.0 ± 3.1 N=15
Feed Consumption (pnd 43 to 44) (g/kg/day)[a]			
	95.9 ‡ ± 2.4 N=14	104.2 * ± 1.7 N=15	97.0 ± 2.6 N=15
Feed Consumption (pnd 44 to 45) (g/kg/day)[a]			
	94.7 ± 1.2 N=14	98.2 ± 3.2 N=15	98.3 ± 2.0 N=14[d]
Feed Consumption (pnd 45 to 46) (g/kg/day)[a]			
	96.2 ± 1.8 N=14	99.5 ± 1.9 N=14[b]	94.1 ± 1.8 N=14[b]
Feed Consumption (pnd 46 to 47) (g/kg/day)[a]			
	91.6 ± 2.0 § N=13[b]	94.1 ± 2.2 N=15	98.7 ± 2.3 N=15
Feed Consumption (pnd 47 to 48) (g/kg/day)[a]			
#	87.3 ††† ± 1.2 Ÿ N=13[b]	94.3 ÞÞÞ ± 1.2 N=15	92.5 Þ ± 1.9 N=15
Feed Consumption (pnd 48 to 49) (g/kg/day)[a]			
	87.6 ± 2.2 N=14	91.9 ± 2.0 N=15	88.1 ± 1.9 N=15
Feed Consumption (pnd 49 to 50) (g/kg/day)[a]			
	86.7 ± 1.9 N=14	89.9 ± 2.0 N=15	86.2 ± 2.9 N=15

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 8 of 9)

	Linuron (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 50 to 51) (g/kg/day)[a]			
	86.7 ± 1.5 N=14	88.9 ± 1.1 N=15	87.5 ± 1.7 N=15
Feed Consumption (pnd 51 to 52) (g/kg/day)[a]			
	81.0 ± 1.3 N=14	84.5 ± 1.9 N=15	80.2 ± 2.8 N=15
Feed Consumption (pnd 52 to 53) (g/kg/day)[a,e]			
	78.1 ± 1.5 N=5	80.2 ± 1.9 N=5	79.0 ± 3.3 N=5
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[a]			
	107.3 ± 0.9 N=12[f]	109.2 ± 1.0 N=14[f]	106.7 ± 1.4 N=13[f]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[a,e]			
	103.7 ± 1.1 N=5	105.6 ± 1.3 N=5	102.2 ± 1.3 N=5

(continued)

Table 4-G. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Linuron Treated F_1 Males (page 9 of 9)

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrease in N is due to the feed consumption value for one or more animals being a statistical outlier and therefore it was excluded.
[c]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[c]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[f]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡ $p<0.05$; ANOVA Test.
‡‡ $p<0.01$; ANOVA Test.
‡‡‡ $p<0.001$; ANOVA Test.
§ $p<0.05$; Test for Linear Trend.
§§ $p<0.01$; Test for Linear Trend.
§§§ $p<0.001$; Test for Linear Trend.
* $p<0.05$; Dunnett's Test.
** $p<0.01$; Dunnett's Test.
*** $p<0.001$; Dunnett's Test.
†† $p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
††† $p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
Ÿ $p<0.05$; Linear trend test in robust regression model.
ŸŸ $p<0.01$; Linear trend test in robust regression model.
Þ $p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model.
ÞÞ $p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
ÞÞÞ $p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 1 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	5.7 ‡‡‡ ± 0.4 §§ N=15	8.3 *** ± 0.3 N=15	7.6 ** ± 0.5 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	10.1 ± 0.3 N=15	10.1 ± 0.7 N=15	9.5 ± 0.7 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	10.3 ‡‡ ± 0.2 N=13[b]	11.9 ** ± 0.4 N=15	10.9 ± 0.3 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	12.1 ± 0.4 N=14[b]	12.4 ± 0.2 N=15	11.9 ± 0.3 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	11.8 ‡ ± 0.3 § N=15	12.7 ± 0.3 N=15	12.9 * ± 0.3 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	12.8 ‡ ± 0.3 § N=15	13.5 ± 0.3 N=15	14.0 * ± 0.3 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
#	15.0 ± 0.8 N=15	15.3 ± 0.4 N=15	15.5 ± 0.4 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	14.1 ± 0.3 N=15	14.5 ± 0.4 N=15	14.6 ± 0.4 N=15
Feed Consumption (pnd 29 to 30) (g/day)[a]			
	14.4 ± 0.5 N=15	15.1 ± 0.3 N=15	15.8 ± 0.8 N=15

(continued)

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 2 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 30 to 31) (g/day)[a]			
	15.6 ± 0.5 N=14[c]	15.7 ± 0.4 N=15	16.3 ± 0.4 N=14[b]
Feed Consumption (pnd 31 to 32) (g/day)[a]			
	17.5 ± 0.6 N=14	17.0 ± 0.4 N=15	16.3 ± 0.5 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]			
	18.5 ± 0.8 N=14	17.7 ± 0.7 N=15	18.3 ± 0.8 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]			
	18.5 ± 0.4 N=14	18.1 ± 0.4 N=15	18.4 ± 0.7 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]			
	19.6 ± 1.1 N=14	20.0 ± 0.5 N=14[b]	19.3 ± 0.8 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]			
	20.4 ± 0.8 N=14	20.6 ± 0.8 N=15	19.8 ± 0.5 N=15
Feed Consumption (pnd 36 to 37) (g/day)[a]			
#	21.9 ± 0.4 N=14	22.9 ± 0.7 N=14[b]	22.4 ± 1.1 N=15
Feed Consumption (pnd 37 to 38) (g/day)[a]			
	22.3 ± 0.6 N=14	23.8 ± 0.6 N=14[b]	21.9 ± 1.3 N=15
Feed Consumption (pnd 38 to 39) (g/day)[a]			
	22.8 ± 0.6 N=14	23.2 ± 1.2 N=14[d]	22.2 ± 1.0 N=15

(continued)

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 3 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 39 to 40) (g/day)[a]	22.9 ± 0.5 N=14	23.5 ± 1.0 N=15	23.2 ± 1.1 N=15
Feed Consumption (pnd 40 to 41) (g/day)[a]	22.8 ± 0.5 N=14	22.6 ± 1.7 N=15	22.2 ± 0.6 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a]	24.3 ± 0.7 N=14	26.4 ± 0.8 N=14[b]	25.2 ± 0.8 N=15
Feed Consumption (pnd 42 to 43) (g/day)[a]	23.3 ± 0.8 N=14	25.0 ± 1.1 N=15	24.4 ± 0.7 N=15
Feed Consumption (pnd 43 to 44) (g/day)[a]	23.1 ± 0.8 N=14	25.0 ± 0.9 N=14[b]	24.2 ± 0.6 N=15
Feed Consumption (pnd 44 to 45) (g/day)[a]	23.6 ± 0.5 N=14	25.1 ± 0.6 N=15	24.0 ± 0.8 N=15
Feed Consumption (pnd 45 to 46) (g/day)[a]	25.0 ± 0.8 N=14	25.6 ± 0.9 N=15	25.3 ± 0.7 N=15
Feed Consumption (pnd 46 to 47) (g/day)[a]	24.9 ± 0.5 N=13[b]	25.8 ± 0.9 N=15	26.4 ± 0.6 N=15
Feed Consumption (pnd 47 to 48) (g/day)[a]	24.6 ± 0.5 N=13[b]	24.8 ± 0.9 N=15	24.8 ± 0.7 N=15

(continued)

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 4 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 48 to 49) (g/day)[a]	25.2 ± 0.9 N=14	24.8 ± 0.8 N=15	25.2 ± 0.9 N=15
Feed Consumption (pnd 49 to 50) (g/day)[a]	25.8 ± 0.9 N=14	26.5 ± 1.0 N=14[b]	26.3 ± 0.8 N=15
Feed Consumption (pnd 50 to 51) (g/day)[a]	26.6 ± 0.8 N=14	27.7 ± 1.0 N=14[d]	27.1 ± 0.9 N=15
Feed Consumption (pnd 51 to 52) (g/day)[a]	25.6 ± 0.7 N=14	25.7 ± 1.0 N=15	23.7 ± 0.8 N=15
Feed Consumption (pnd 52 to 53) (g/day)[a,e]	25.9 ± 1.0 N=5	26.9 ± 2.5 N=5	27.2 ± 2.0 N=3
Feed Consumption (pnd 23 to 52, treatment period) (g/day)[a]	20.5 ± 0.4 N=12[f]	20.9 ± 0.5 N=12[f]	20.5 ± 0.5 N=14[f]
Feed Consumption (pnd 23 to 53, treatment period) (g/day)[a,e]	20.7 ± 0.4 N=5	21.4 ± 1.2 N=5	22.3 ± 0.8 N=2[f]
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	98.2 ‡‡‡ ± 7.0 § N=15	143.5 *** ± 7.8 N=15	130.8 * ± 9.1 N=15
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]	158.7 ± 3.9 N=15	157.6 ± 9.5 N=15	149.0 ± 10.5 N=15

(continued)

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 5 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
	144.5 ‡‡ ± 2.4 N=13[b]	168.2 *** ± 4.4 N=15	155.3 ± 4.8 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	154.9 ± 4.8 N=14	160.5 ± 2.2 N=15	155.8 ± 3.8 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	141.4 ‡‡‡ ± 3.2 §§§ N=15	152.4 * ± 2.2 N=15	158.0 *** ± 3.0 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	142.6 ‡‡‡ ± 2.4 §§§ N=15	150.3 * ± 2.2 N=15	159.1 *** ± 2.4 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	153.1 ± 5.8 N=15	157.5 ± 3.0 N=15	164.9 ± 3.5 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	134.9 ± 3.5 N=15	138.8 ± 4.0 N=15	145.7 ± 5.7 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
	127.3 ‡ ± 2.4 §§ N=15	133.9 ± 1.1 N=15	145.5 ** ± 7.0 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	128.9 ‡‡ ± 2.4 §§ N=14[c]	130.4 ± 2.4 N=15	140.3 ** ± 2.7 N=14[b]
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]			
	134.2 ± 2.3 N=14	132.3 ± 2.0 N=15	132.5 ± 3.0 N=15

(continued)

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 6 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	132.2 ± 3.9 N=14	128.4 ± 3.3 N=15	139.8 ± 5.0 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	124.3 ± 2.6 N=14	124.4 ± 2.0 N=15	132.2 ± 3.6 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	123.7 ± 5.6 N=14	129.3 ± 1.5 N=14[b]	130.2 ± 4.1 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	121.9 ± 2.8 N=14	125.1 ± 5.1 N=15	125.6 ± 2.3 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	123.5 ± 1.7 § N=14	130.9 ± 2.3 N=14[b]	133.5 ± 4.9 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
	118.7 ± 1.7 N=14	128.3 ± 3.2 N=14[b]	124.8 ± 7.7 N=15
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
	115.9 ± 3.0 N=14	119.5 ± 5.5 N=14[d]	119.6 ± 3.7 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
	111.3 ± 1.9 N=14	114.6 ± 4.4 N=15	119.3 ± 4.8 N=15
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
	106.5 ± 2.0 N=14	105.3 ± 6.8 N=15	109.2 ± 2.0 N=15

(continued)

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 7 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]	108.8 ‡‡ ± 2.5 §§ N=14	118.1 * ± 2.7 N=14[b]	119.1 ** ± 2.0 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[a]	100.4 ± 3.0 N=14	108.5 ± 5.3 N=15	110.9 ± 2.1 N=15
Feed Consumption (pnd 43 to 44) (g/kg/day)[a]	95.9 ‡‡ ± 2.4 §§ N=14	103.9 * ± 2.3 N=14[b]	105.6 ** ± 1.5 N=15
Feed Consumption (pnd 44 to 45) (g/kg/day)[a]	94.7 ± 1.2 § N=14	101.3 ± 2.4 N=15	101.5 ± 2.6 N=15
Feed Consumption (pnd 45 to 46) (g/kg/day)[a]	96.2 ± 1.8 § N=14	99.2 ± 2.3 N=15	102.8 ± 1.5 N=15
Feed Consumption (pnd 46 to 47) (g/kg/day)[a]	91.6 ‡‡‡ ± 2.0 §§§ N=13[b]	96.7 ± 2.1 N=15	103.9 *** ± 1.7 N=15
Feed Consumption (pnd 47 to 48) (g/kg/day)[a]	87.3 ± 1.2 § N=13[b]	90.5 ± 2.4 N=15	94.7 ± 2.3 N=15
Feed Consumption (pnd 48 to 49) (g/kg/day)[a]	87.6 ± 2.2 § N=14	87.9 ± 1.2 N=15	92.9 ± 1.8 N=15
Feed Consumption (pnd 49 to 50) (g/kg/day)[a]	86.7 ‡ ± 1.9 §§ N=14	90.1 ± 2.0 N=14[b]	94.0 ** ± 1.4 N=15

(continued)

Table 4-H. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Phenobarbital Treated F_1 Males (page 8 of 8)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 50 to 51) (g/kg/day)[a]			
	86.7 ± 1.5 **§** N=14	91.2 ± 2.1 N=14[d]	94.3 ± 2.6 N=15
Feed Consumption (pnd 51 to 52) (g/kg/day)[a]			
	81.0 ± 1.3 N=14	82.3 ± 2.7 N=15	79.9 ± 2.2 N=15
Feed Consumption (pnd 52 to 53) (g/kg/day)[a,e]			
	78.1 ± 1.5 N=5	83.5 ± 3.5 N=5	83.6 ± 3.2 N=3
Feed Consumption (pnd 23 to 52, treatment period) (g/kg/day)[a]			
	107.3 **‡‡‡** ± 0.9 **§§§** N=12[f]	111.4 ****** ± 1.1 N=12[f]	114.9 ******* ± 0.7 N=14[f]
Feed Consumption (pnd 23 to 53, treatment period) (g/kg/day)[a,e]			
	103.7 **‡** ± 1.1 **§§** N=5	110.8 ***** ± 2.3 N=5	112.4 ***** ± 1.0 N=2[f]

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrease in N is due to the feed consumption value for one or more animals being a statistical outlier and therefore it was excluded.
[c]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[c]Decrease in N is due to the feed consumption value for one animal being unrealistic (i.e. negative) and therefore it was excluded.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 53.
[f]Decrease in N is due to interim feed consumption value(s) for one or more animals being missing and therefore the overall feed consumption value could not be calculated.
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡$p<0.05$; ANOVA Test.
‡‡$p<0.01$; ANOVA Test.
‡‡‡$p<0.001$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§$p<0.01$; Test for Linear Trend.
§§§$p<0.001$; Test for Linear Trend.
*****$p<0.05$; Dunnett's Test.
******$p<0.01$; Dunnett's Test.
*******$p<0.001$; Dunnett's Test.

Table 5-A. Summary of Clinical Observations During the Post Wean Period for the Atrazine-Treated F_1 Males (page 1 of 3)

A. Clinical Observations Summarized by Group	Atrazine (mg/kg/day, po)		
Observation	0	75	150
Efflux of the dosing solution		4	2
Found dead after dosing		1	
Rooting: post dosing		6	11
Rooting: prior to dosing			2
Rust colored fur			1
Salivation: post dosing			1
Salivation: prior to dosing	2	8	12

B. Clinical Observations Summarized by Group and Day		Atrazine (mg/kg/day, po)		
Day[a]	Observation[b]	0	75	150
24	Efflux of the dosing solution			1
25	Efflux of the dosing solution		1	
29	Rooting: post dosing			1
	Salivation: prior to dosing		1	1
30	Rooting: post dosing			1
	Salivation: prior to dosing		1	1
31	Salivation: prior to dosing		1	1
32	Rooting: post dosing			3
	Salivation: prior to dosing		1	2
33	Rooting: post dosing			4
	Salivation: prior to dosing		4	3
34	Rooting: post dosing			4
	prior to dosing			1
	Salivation: prior to dosing		3	2
35	Rooting: post dosing			5
	prior to dosing			1
	Salivation: prior to dosing		3	3
36	Rooting: post dosing			2
	Salivation: prior to dosing		2	2

(continued)

Table 5-A. Summary of Clinical Observations During the Post Wean Period for the Atrazine-Treated F_1 Males (page 2 of 3)

B. Clinical Observations Summarized by Group and Day		Atrazine (mg/kg/day, po)		
Day[a]	Observation[b]	0	75	150
37	Efflux of the dosing solution		1	
	Found dead after dosing		1	
	Rooting: post dosing			3
	Salivation: prior to dosing		5	6
38	Rooting: post dosing			6
	Salivation: prior to dosing		6	7
39	Efflux of the dosing solution			1
	Efflux of the dosing solution, slight		1	
	Rooting: post dosing		3	4
	Salivation: prior to dosing		5	6
40	Rooting: post dosing		2	3
	Salivation: prior to dosing		3	3
41	Rooting: post dosing		1	3
	Salivation: prior to dosing		4	6
42	Rooting: post dosing			3
	Salivation: prior to dosing		3	8
43	Efflux of the dosing solution			1
	Rooting: post dosing		3	4
	Salivation: prior to dosing		4	7
44	Rooting: post dosing		1	9
	Salivation: post dosing			1
	prior to dosing		5	6
45	Rooting: post dosing		2	4
	prior to dosing			1
	Salivation: prior to dosing		2	11
46	Rooting: post dosing		2	5
	Salivation: post dosing			1
	prior to dosing		4	4
47	Efflux of the dosing solution		1	
	Rooting: post dosing		1	5
	Salivation: post dosing			1
	prior to dosing	2	3	3
48	Rooting: post dosing		2	7
	Rust colored fur: chin			1
	Salivation: prior to dosing		1	5

(continued)

Table 5-A. Summary of Clinical Observations During the Post Wean Period for the Atrazine-Treated F_1 Males (page 3 of 3)

B. Clinical Observations Summarized by Group and Day		Atrazine (mg/kg/day, po)		
Day[a]	Observation[b]	0	75	150
49	Rooting: post dosing		2	7
	Rust colored fur: chin			1
	Salivation: prior to dosing		2	6
50	Efflux of the dosing solution			1
	Efflux of the dosing solution, small amount		1	
	Rooting: post dosing		1	4
	Rust colored fur: chin			1
	Salivation: prior to dosing		3	4
51	Rooting: post dosing		1	1
	Salivation: prior to dosing		1	3
52	Rooting: post dosing		1	3
	Salivation: prior to dosing			3

[a]Postnatal day.
[b]Clinical observations are tabulated once per day per animal.

Table 5-B. Summary of Clinical Observations During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene-Treated F_1 Males (page 1 of 2)

A. Clinical Observations Summarized by Group	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
Observation	0	50	100
Chromodacryorrhea		1	1
Efflux of the dosing solution			1
Euthanized after dosing due to a leg injury		1	
Injury of the left rear leg, swelling of the left metatarsal area, possible fracture but not evident		1	
Rooting: post dosing		1	9
Rust colored fur		1	
Salivation: prior to dosing	2	1	3

B. Clinical Observations Summarized by Group and Day		p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
26	Efflux of the dosing solution			1
	Injury of the left rear leg, swelling of the left metatarsal area, possible fracture but not evident		1	
27	Injury of the left rear leg, swelling of the left metatarsal area, possible fracture but not evident		1	
28	Injury of the left rear leg, swelling of the left metatarsal area, possible fracture but not evident		1	
29	Injury of the left rear leg, increased swelling of the left metatarsal area, possible fracture but not evident; euthanized after dosing		1	
	Rooting: post dosing		1	1
	Salivation: prior to dosing		1	
31	Rooting: post dosing			1
	Salivation: prior to dosing		1	1
32	Rooting: post dosing		1	
	Salivation: prior to dosing		1	
34	Chromodacryorrhea: nose		1	
	Salivation: prior to dosing		1	
35	Rooting: post dosing		1	5
	Salivation: prior to dosing		1	
36	Rooting: post dosing			1
37	Rooting: post dosing			2
	Salivation: prior to dosing		1	

(continued)

Table 5-B. Summary of Clinical Observations During the Post Wean Period for the p,p'-Dichlorodiphenyldichloroethylene-Treated F_1 Males (page 2 of 2)

B. Clinical Observations Summarized by Group and Day		p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
38	Rooting: post dosing			2
	Salivation: prior to dosing		1	
39	Rooting: post dosing			2
	Salivation: prior to dosing		1	
40	Rooting: post dosing			2
	Salivation: prior to dosing		1	1
41	Rooting: post dosing			1
	Salivation: prior to dosing		1	
42	Salivation: prior to dosing		1	
43	Efflux of the dosing solution, slight			1
	Rooting: post dosing			2
	Rust colored fur: back		1	
	Salivation: prior to dosing		1	
44	Chromodacryorrhea: eye, right			1
	Rust colored fur: back		1	
45	Chromodacryorrhea: eye, right			1
	Rooting: post dosing			2
	Salivation: prior to dosing		1	1
46	Chromodacryorrhea: eye, right			1
47	Chromodacryorrhea: eye, right			1
	Salivation: prior to dosing	2	1	
48	Chromodacryorrhea: eye, right, gone			1
49	Rooting: post dosing			1
	Salivation: prior to dosing		1	

[a]Postnatal day.
[b]Clinical observations are tabulated once per day per animal.

Table 5-C. Summary of Clinical Observations During the Post Wean Period for the Vinclozolin-Treated F_1 Males (page 1 of 2)

A. Clinical Observations Summarized by Group	Vinclozolin (mg/kg/day, po)		
Observation	0	30	100
Animal not dosed, no dosing solution available		2	
Efflux of the dosing solution		1	3
Piloerection			1
Rooting: post dosing		4	4
Salivation: prior to dosing	2	2	5
Sore(s)		1	

B. Clinical Observations Summarized by Group and Day		Vinclozolin (mg/kg/day, po)		
Day[a]	Observation[b]	0	30	100
25	Efflux of the dosing solution			2
	Piloerection			1
26	Rooting: post dosing			1
29	Efflux of the dosing solution			1
	Salivation: prior to dosing			2
30	Salivation: prior to dosing			2
32	Salivation: prior to dosing			1
33	Salivation: prior to dosing			1
34	Salivation: prior to dosing			2
35	Rooting: post dosing		1	
	Salivation: prior to dosing			1
36	Salivation: prior to dosing		1	1
37	Rooting: post dosing			1
	Salivation: prior to dosing		1	2
38	Efflux of the dosing solution, slight			1
	Rooting: post dosing			1
	Salivation: prior to dosing		1	3

(continued)

Table 5-C. Summary of Clinical Observations During the Post Wean Period for the Vinclozolin-Treated F_1 Males (page 2 of 2)

B. Clinical Observations Summarized by Group and Day		Vinclozolin (mg/kg/day, po)		
Day[a]	Observation[b]	0	30	100
39	Efflux of the dosing solution, slight		1	
	Rooting: post dosing			1
	Salivation: prior to dosing			3
40	Rooting: post dosing			2
	Salivation: prior to dosing			3
41	Rooting: post dosing		1	1
	Salivation: prior to dosing			2
43	Rooting: post dosing		2	
	Salivation: prior to dosing			1
44	Rooting: post dosing		1	1
	Salivation: prior to dosing			2
45	Rooting: post dosing			1
	Salivation: prior to dosing			2
46	Efflux of the dosing solution			1
	Rooting: post dosing			1
	Sore(s): neck		1	
47	Salivation: prior to dosing	2		
	Sore(s): neck		1	
48	Sore(s): neck		1	
49	Rooting: post dosing			1
	Sore(s): neck		1	
50	Animal not dosed, no dosing solution available		2	
	Sore(s): neck, healed		1	
51	Salivation: prior to dosing			1

[a]Postnatal day.
[b]Clinical observations are tabulated once per day per animal.

Table 5-D. Summary of Clinical Observations During the Post Wean Period for the Methoxychlor-Treated F_1 Males (page 1 of 1)

A. Clinical Observations Summarized by Group	Methoxychlor (mg/kg/day, po)		
Observation	0	25	50
Chromodacryorrhea		1	
Efflux of the dosing solution		2	1
Rooting: post dosing			2
Salivation: prior to dosing	2		

B. Clinical Observations Summarized by Group and Day		Methoxychlor (mg/kg/day, po)		
Day[a]	Observation[b]	0	25	50
23	Efflux of the dosing solution		2	1
30	Rooting: post dosing			1
34	Chromodacryorrhea: nose		1	
44	Rooting: post dosing			1
45	Rooting: post dosing			1
47	Salivation: prior to dosing	2		
48	Rooting: post dosing			1

[a]Postnatal day.
[b]Clinical observations are tabulated once per day per animal.

Table 5-E. Summary of Clinical Observations During the Post Wean Period for the Propylthiouracil-Treated F_1 Males (page 1 of 2)

A. Clinical Observations Summarized by Group	Propylthiouracil (mg/kg/day, po)		
Observation	0	2	25
Efflux of the dosing solution		1	1
Found dead prior to dosing	1		1
Rooting: post dosing		2	14
Rough coat		1	
Salivation: prior to dosing		1	1

B. Clinical Observations Summarized by Group and Day		Propylthiouracil (mg/kg/day, po)		
Day[a]	Observation[b]	0	2	25
30	Rooting: post dosing			5
	Rough coat		1	
31	Found dead prior to dosing	1		
	Rooting: post dosing			4
32	Rooting: post dosing		1	7
33	Rooting: post dosing			11
34	Rooting: post dosing			4
35	Rooting: post dosing			1
	Salivation: prior to dosing		1	
36	Rooting: post dosing			2
37	Rooting: post dosing			6
38	Efflux of the dosing solution		1	
	Rooting: post dosing			7
	Salivation: prior to dosing			1
39	Rooting: post dosing		1	5
40	Rooting: post dosing			2
41	Rooting: post dosing			5
42	Rooting: post dosing			1
43	Rooting: post dosing			1
44	Rooting: post dosing			3
	Salivation: prior to dosing			1

(continued)

Table 5-E. Summary of Clinical Observations During the Post Wean Period for the Propylthiouracil-Treated F_1 Males (page 2 of 2)

B. Clinical Observations Summarized by Group and Day		Propylthiouracil (mg/kg/day, po)		
Day[a]	Observation[b]	0	2	25
45	Efflux of the dosing solution			1
	Rooting: post dosing			4
46	Rooting: post dosing			1
47	Rooting: post dosing			6
48	Rooting: post dosing			7
	Salivation: prior to dosing			1
49	Rooting: post dosing			3
50	Efflux of the dosing solution			1
	Found dead prior to dosing			1
	Rooting: post dosing			1
51	Rooting: post dosing			1

[a]Postnatal day.
[b]Clinical observations are tabulated once per day per animal.

Table 5-F. Summary of Clinical Observations During the Post Wean Period for the Ketoconazole-Treated F_1 Males (page 1 of 3)

A. Clinical Observations Summarized by Group	Ketoconazole (mg/kg/day, po)		
Observation	0	50	100
Efflux of the dosing solution		1	1
Found dead prior to dosing	1		1
Piloerection			1
Rooting: post dosing		14	15
Rooting: prior to dosing		1	
Rough coat		1	2
Salivation: prior to dosing		4	13

B. Clinical Observations Summarized by Group and Day		Ketoconazole (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
24	Efflux of the dosing solution		1	
25	Efflux of the dosing solution			1
	Salivation: prior to dosing			1
26	Rooting: post dosing			9
27	Rooting: post dosing		4	10
	Salivation: prior to dosing			1
28	Rooting: post dosing		2	4
	Salivation: prior to dosing			1
29	Rough coat			1
30	Rooting: post dosing		1	
	Rough coat			2
31	Found dead prior to dosing	1		
	Rooting: post dosing		2	5
	prior to dosing		1	
32	Rooting: post dosing		1	7
	Rough coat			1
	Salivation: prior to dosing			2
33	Rooting: post dosing		1	7
	Rough coat			1
	Salivation: prior to dosing			3
34	Rooting: post dosing		1	6
	Rough coat		1	1
	Salivation: prior to dosing		2	9

(continued)

Table 5-F. Summary of Clinical Observations During the Post Wean Period for the Ketoconazole-Treated F_1 Males (page 2 of 3)

B. Clinical Observations Summarized by Group and Day		Ketoconazole (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
35	Rooting: post dosing		3	5
	Rough coat			1
	Salivation: prior to dosing			1
36	Piloerection			1
	Rooting: post dosing		3	7
	Rough coat			1
	Salivation: prior to dosing			3
37	Found dead prior to dosing			1
	Rooting: post dosing		9	9
	Rough coat			1
	Salivation: prior to dosing			2
38	Rooting: post dosing		10	11
	Rough coat			1
	Salivation: prior to dosing			3
39	Rooting: post dosing		9	5
	Rough coat			1
	Salivation: prior to dosing			2
40	Rooting: post dosing		4	7
	Rough coat			1
	Salivation: prior to dosing		1	5
41	Rooting: post dosing		1	9
	Salivation: prior to dosing		2	4
42	Rooting: post dosing			4
	Salivation: prior to dosing		1	1
43	Rooting: post dosing			2
	Salivation: prior to dosing			1
44	Rooting: post dosing		1	3
	Salivation: prior to dosing		1	1
45	Rooting: post dosing		4	7
	Salivation: prior to dosing			1
46	Rooting: post dosing		5	5
	Salivation: prior to dosing			1
47	Rooting: post dosing		1	4
	Salivation: prior to dosing			2

(continued)

Table 5-F. Summary of Clinical Observations During the Post Wean Period for the Ketoconazole-Treated F_1 Males (page 3 of 3)

B. Clinical Observations Summarized by Group and Day		Ketoconazole (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
48	Rooting: post dosing		1	8
	Salivation: prior to dosing			6
49	Rooting: post dosing			1
	Salivation: prior to dosing			4
50	Rooting: post dosing		1	4
	Salivation: prior to dosing			3
51	Rooting: post dosing			2
	Salivation: prior to dosing			3
52	Salivation: prior to dosing			2

[a]Postnatal day.
[b]Clinical observations are tabulated once per day per animal.

Table 5-G. Summary of Clinical Observations During the Post Wean Period for the Linuron-Treated F_1 Males (page 1 of 2)

A. Clinical Observations Summarized by Group	Linuron (mg/kg/day, po)		
Observation	0	50	100
Difficult to dose			1
Efflux of the dosing solution			1
Found dead prior to dosing	1		
Rooting: post dosing		15	15
Salivation: post dosing		1	
Salivation: prior to dosing		6	14

B. Clinical Observations Summarized by Group and Day		Linuron (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
25	Efflux of the dosing solution			1
	Rooting: post dosing			5
26	Rooting: post dosing			11
	Salivation: prior to dosing			1
27	Rooting: post dosing			15
28	Rooting: post dosing			5
29	Rooting: post dosing			1
	Salivation: prior to dosing			3
30	Rooting: post dosing		4	10
	Salivation: prior to dosing		2	4
31	Found dead prior to dosing	1		
	Rooting: post dosing		7	14
	Salivation: prior to dosing		1	3
32	Rooting: post dosing		7	13
	Salivation: prior to dosing		1	6
33	Rooting: post dosing		14	12
	Salivation: prior to dosing		1	5
34	Rooting: post dosing		6	12
	Salivation: prior to dosing		1	4
35	Rooting: post dosing		3	10
	Salivation: prior to dosing			1
36	Rooting: post dosing		2	12
	Salivation: prior to dosing			1

(continued)

Table 5-G. Summary of Clinical Observations During the Post Wean Period for the Linuron-Treated F_1 Males (page 2 of 2)

B. Clinical Observations Summarized by Group and Day		Linuron (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
37	Rooting: post dosing		9	12
	Salivation: prior to dosing		2	4
38	Rooting: post dosing		9	15
	Salivation: prior to dosing		3	6
39	Rooting: post dosing		11	14
	Salivation: prior to dosing		1	3
40	Rooting: post dosing		10	11
	Salivation: prior to dosing		2	9
41	Difficult to dose			1
	Rooting: post dosing		7	10
	Salivation: prior to dosing		2	7
42	Rooting: post dosing		4	5
	Salivation: prior to dosing		3	5
43	Rooting: post dosing		5	1
	Salivation: prior to dosing		5	2
44	Rooting: post dosing		9	11
	Salivation: prior to dosing		4	6
45	Rooting: post dosing		7	7
	Salivation: prior to dosing		5	4
46	Rooting: post dosing		4	4
	Salivation: prior to dosing		2	4
47	Rooting: post dosing		10	7
	Salivation: prior to dosing		2	3
48	Rooting: post dosing		10	9
	Salivation: prior to dosing		2	2
49	Rooting: post dosing		5	2
	Salivation: prior to dosing		1	1
50	Rooting: post dosing		3	7
	Salivation: prior to dosing		1	1
51	Rooting: post dosing		7	5
	Salivation: post dosing		1	
	prior to dosing		1	1
52	Salivation: prior to dosing			1

[a] Postnatal day.
[b] Clinical observations are tabulated once per day per animal.

Table 5-H. Summary of Clinical Observations During the Post Wean Period for the Phenobarbital-Treated F_1 Males (page 1 of 3)

A. Clinical Observations Summarized by Group	Phenobarbital (mg/kg/day, po)		
Observation	0	50	100
Ataxia: post dosing		6	5
Efflux of the dosing solution		1	1
Found dead prior to dosing	1		
Prone: post dosing		4	15
Right front leg: bruised			1
Right front paw: second digit missing			1
Rooting: post dosing		12	15
Rough coat		4	3
Salivation: prior to dosing		4	6

B. Clinical Observations Summarized by Group and Day		Phenobarbital (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
23	Ataxia: post dosing		2	3
	Efflux of the dosing solution		1	
	Prone: post dosing		1	9
24	Ataxia: post dosing		3	2
	Efflux of the dosing solution			1
	Prone: post dosing		4	15
25	Ataxia: post dosing		1	
	Prone: post dosing			6
26	Rooting: post dosing		4	8
	Salivation: prior to dosing		1	1
27	Rooting: post dosing		5	13
	Salivation: prior to dosing		1	2
28	Rooting: post dosing		2	6
30	Right front leg: bruised, animal not using it			1
	Rooting: post dosing		3	2
31	Found dead prior to dosing	1		
	Right front leg: bruised, animal using it a little			1
	Rooting: post dosing		4	4
32	Right front leg: bruised, animal using it			1
	Rooting: post dosing		1	11
	Salivation: prior to dosing		1	3
33	Rooting: post dosing		3	5
	Rough coat		2	2
	Salivation: prior to dosing		1	2

(continued)

Table 5-H. Summary of Clinical Observations During the Post Wean Period for the Phenobarbital-Treated F_1 Males (page 2 of 3)

B. Clinical Observations Summarized by Group and Day		Phenobarbital (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
34	Rooting: post dosing		4	4
	Rough coat		2	
	Salivation: prior to dosing		1	3
35	Rooting: post dosing		3	7
	Rough coat		1	
	Salivation: prior to dosing			1
36	Rooting: post dosing		2	7
	Rough coat		1	
37	Rooting: post dosing		5	10
	Rough coat			1
	Salivation: prior to dosing		1	
38	Rooting: post dosing		6	11
	Rough coat		1	1
	Salivation: prior to dosing		1	2
39	Rooting: post dosing		5	11
	Rough coat		1	1
	Salivation: prior to dosing		1	3
40	Right front paw: second digit missing			1
	Rooting: post dosing		6	7
	Salivation: prior to dosing		3	4
41	Right front paw: second digit missing			1
	Rooting: post dosing		6	7
	Salivation: prior to dosing		1	1
42	Right front paw: second digit missing			1
	Rooting: post dosing		2	5
43	Right front paw: second digit missing			1
	Rooting: post dosing		1	2
45	Rooting: post dosing		1	
46	Rooting: post dosing			1
47	Rooting: post dosing		2	4
48	Rooting: post dosing		3	3
	Salivation: prior to dosing		1	1
49	Rooting: post dosing		2	4

(continued)

Table 5-H. Summary of Clinical Observations During the Post Wean Period for the Phenobarbital-Treated F_1 Males (page 3 of 3)

B. Clinical Observations Summarized by Group and Day		Phenobarbital (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
50	Salivation: prior to dosing		1	1
51	Rooting: post dosing		1	

[a]Postnatal day.
[b]Clinical observations are tabulated once per day per animal.

Table 6-A. Summary and Statistical Analysis of the Preputial Separation Data for the Atrazine-Treated F_1 Males (page 1 of 1)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Males on Study	12[a]	13[b]	12[c]
Number of Males Evaluated	12	12[d]	12
Average Postnatal Day of Preputial Separation[e]	41.4 ± 0.7 N=12	42.0 ± 0.5 N=12	42.9 ± 0.4 N=12
Average Body Weight (g) on Day of Acquisition[e]	219.50 ‡ ± 5.79 §§ N=12	208.84 ± 5.57 N=12	200.26 * ± 2.64 N=12

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 18 was removed from the study because it was not dosed on the correct postnatal days and male 119 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Males 55, 118 and 127 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Male 54 was found dead on postnatal day 37 after dosing (misdirected dose).
[e]Reported as the mean ± S.E.M.; pnd = postnatal day.
‡$p<0.05$; ANOVA Test.
§§$p<0.01$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.

Table 6-B. Summary and Statistical Analysis of the Preputial Separation Data for the p,p'-Dichlorodiphenyldichloroethylene-Treated F_1 Males (page 1 of 1)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
No. of Males on Study	12[a]	14[b]	15
Number of Males Evaluated	12	13[c]	15
Average Postnatal Day of Preputial Separation[d]	41.4 ‡‡‡ ± 0.7 §§§ N=12	44.9 *** ± 0.3 N=13	45.7 *** ± 0.4 N=15
Average Body Weight (g) on Day of Acquisition[d]	219.50 ‡‡‡ ± 5.79 §§§ N=12	251.10 *** ± 6.35 N=13	259.19 *** ± 4.58 N=15

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 74 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Male 20 was euthanized on postnatal day 29 after dosing due to a leg injury.
[d]Reported as the mean ± S.E.M.; pnd = postnatal day.
‡‡‡p<0.001; ANOVA Test.
§§§p<0.001; Test for Linear Trend.
***p<0.001; Dunnett's Test.

Table 6-C. Summary and Statistical Analysis of the Preputial Separation Data for the Vinclozolin-Treated F_1 Males (page 1 of 1)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
No. of Males on Study	12[a]	13[b]	12[c]
Number of Males Evaluated	12	13	10[d]
Average Postnatal Day of Preputial Separation[e]	41.4 ‡‡‡ ± 0.7 §§§ N=12	43.8 ** ± 0.3 N=13	46.8 *** ± 0.3 N=10
Average Body Weight (g) on Day of Acquisition[e]	219.50 ‡‡‡ ± 5.79 §§§ N=12	242.86 ** ± 4.97 N=13	259.64 *** ± 5.98 N=10

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 79 and 115 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Males 24, 114 and 131 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Males 9 and 59 were not positive for preputial separation by postnatal day 52 when they were necropsied and therefore they were excluded from the evaluation.
[e]Reported as the mean ± S.E.M.; pnd = postnatal day.
‡‡‡p<0.001; ANOVA Test.
§§§p<0.001; Test for Linear Trend.
**p<0.01; Dunnett's Test.
***p<0.001; Dunnett's Test.

Table 6-D. Summary and Statistical Analysis of the Preputial Separation Data for the Methoxychlor-Treated F_1 Males (page 1 of 1)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Males on Study	12[a]	15	13[b]
Number of Males Evaluated	12	14[c]	13
Average Postnatal Day of Preputial Separation[d]	41.4 ± 0.7 N=12	41.8 ± 0.7 N=14	41.8 ± 0.6 N=13
Average Body Weight (g) on Day of Acquisition[d]	219.50 ± 5.79 N=12	218.70 ± 4.33 N=14	220.46 ± 6.32 N=13

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 17 and 30 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Male 134 was not positive for preputial separation by postnatal day 53 when it was necropsied and therefore it was excluded from the evaluation.
[d]Reported as the mean ± S.E.M.; pnd = postnatal day.

Table 6-E. Summary and Statistical Analysis of the Preputial Separation Data for the Propylthiouracil-Treated F_1 Males (page 1 of 1)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Males on Study	15	15	15
Number of Males Evaluated	14[a]	15	15
Average Postnatal Day of Preputial Separation[b]	39.6 ‡‡‡ §§§ ± 0.4 N=14	40.4 ± 0.4 N=15	43.3 *** ± 0.5 N=15
Average Body Weight (g) on Day of Acquisition[b]	207.47 ‡‡‡ §§§ ± 4.20 N=14	216.75 ± 4.75 N=15	166.54 *** ± 3.95 N=15

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Reported as the mean ± S.E.M.; pnd = postnatal day.
‡‡‡p<0.001; ANOVA Test.
§§§p<0.001; Test for Linear Trend.
***p<0.001; Dunnett's Test.

Table 6-F. Summary and Statistical Analysis of the Preputial Separation Data for the Ketoconazole-Treated F_1 Males (page 1 of 1)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Number of Males Evaluated	14[a]	15	14[b]
Average Postnatal Day of Preputial Separation[c]			
#	39.6 ††† ± 0.4 ŸŸŸ N=14	42.3 ÞÞÞ ± 0.4 N=15	44.1 ÞÞÞ ± 0.2 N=14
Average Body Weight (g) on Day of Acquisition[c]	207.47 ‡‡ ± 4.20 §§ N=14	227.15 * ± 7.26 N=15	234.76 ** ± 4.98 N=14

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Male 242 was found dead on postnatal day 37 prior to dosing (misdirected dose).
[c]Reported as the mean ± S.E.M.; pnd = postnatal day.
#Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
†††$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸŸ$p<0.001$; Linear trend test in robust regression model.
ÞÞÞ$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.
‡‡$p<0.01$; ANOVA Test.
§§$p<0.01$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.
**$p<0.01$; Dunnett's Test.

Table 6-G. Summary and Statistical Analysis of the Preputial Separation Data for the Linuron-Treated F_1 Males (page 1 of 1)

	Linuron (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Number of Males Evaluated	14[a]	15	15
Average Postnatal Day of Preputial Separation[b]	39.6 ‡‡‡ §§§ ± 0.4 N=14	43.6 *** ± 0.5 N=15	45.5 *** ± 0.4 N=15
Average Body Weight (g) on Day of Acquisition[b]	207.47 ‡ § ± 4.20 N=14	226.64 * ± 3.41 N=15	223.97 * ± 6.41 N=15

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Reported as the mean ± S.E.M.; pnd = postnatal day.
‡p<0.05; ANOVA Test.
‡‡‡p<0.001; ANOVA Test.
§p<0.05; Test for Linear Trend.
§§§p<0.001; Test for Linear Trend.
*p<0.05; Dunnett's Test.
***p<0.001; Dunnett's Test.

Table 6-H. Summary and Statistical Analysis of the Preputial Separation Data for the Phenobarbital-Treated F_1 Males (page 1 of 1)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
Number of Males Evaluated	14[a]	15	15
Average Postnatal Day of Preputial Separation[b]			
#	39.6 ††† ± 0.4 ŸŸŸ N=14	41.3 ÞÞ ± 0.3 N=15	43.0 ÞÞÞ ± 0.5 N=15
Average Body Weight (g) on Day of Acquisition[b]	207.47 ‡ ± 4.20 § N=14	220.48 ± 5.27 N=15	224.17 * ± 4.83 N=15

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Reported as the mean ± S.E.M.; pnd = postnatal day.
#Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
†††$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸŸ$p<0.001$; Linear trend test in robust regression model.
ÞÞ$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
ÞÞÞ$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.
‡$p<0.05$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine Treated F_1 Males (page 1 of 6)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Males on Study	12[a]	13[b]	12[c]
No. of Males at Scheduled Sacrifice	12	12[d]	12
Sacrifice Body Weight (g)[e]			
	316.31 ‡‡‡ ± 6.46 §§§ N=11[f]	279.00 *** ± 4.52 N=12	256.67 *** ± 4.35 N=12
Pituitary Weight (g)[e]			
	0.0113 ‡‡‡ ± 0.0003 §§§ N=12	0.0100 * ± 0.0005 N=12	0.0079 *** ± 0.0005 N=12
Thyroid Weight (g)[e]			
#	0.0185 ± 0.0012 N=12	0.0205 ± 0.0008 N=12	0.0186 ± 0.0007 N=12
Liver Weight (g)[e]			
#	16.4133 †† ± 0.6404 ŸŸŸ N=12	14.8414 Þ ± 0.3419 N=12	13.9548 ÞÞ ± 0.3022 N=12
Paired Adrenal Gland Weight (g)[e]			
	0.0534 ± 0.0025 N=12	0.0497 ± 0.0019 N=12	0.0538 ± 0.0021 N=12
Paired Kidney Weight (g)[e]			
	2.8524 ‡‡ ± 0.0865 §§ N=12	2.7231 ± 0.0537 N=12	2.5378 ** ± 0.0527 N=12
Paired Testis Weight (g)[e]			
	2.7402 ± 0.0497 N=12	2.8174 ± 0.0580 N=12	2.8196 ± 0.0664 N=12
Paired Epididymis Weight (g)[e]			
	0.4856 ‡‡ ± 0.0129 §§ N=12	0.4478 ± 0.0133 N=12	0.4207 ** ± 0.0126 N=12

(continued)

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine Treated F_1 Males (page 2 of 6)

	Atrazine (mg/kg/day, po)		
	0	75	150
Ventral Prostate Weight (g)[e]			
	0.2407 ± 0.0113 §§ N=12	0.2092 ± 0.0145 N=12	0.1969 ± 0.0127 N=12
Dorsolateral Prostate Weight (g)[e]			
	0.1973 ± 0.0167 §§ N=12	0.1796 ± 0.0079 N=12	0.1560 ± 0.0098 N=12
Prostate Weight (g)[e]			
	0.4380 ‡ ± 0.0221 §§ N=12	0.3888 ± 0.0195 N=12	0.3529 ** ± 0.0186 N=12
Seminal Vesicles with Coagulating Glands Weight (g)[e]			
	0.5529 ‡‡ ± 0.0332 §§ N=12	0.4528 * ± 0.0260 N=12	0.4204 ** ± 0.0215 N=12
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[e]			
	0.7060 ‡ ± 0.0259 §§ N=12	0.5961 ± 0.0406 N=12	0.5601 ** ± 0.0335 N=12
Adjusted Pituitary Weight (g)[g]			
	0.0105 ± 0.0006 N=11[f]	0.0101 ± 0.0004 N=12	0.0087 ± 0.0005 N=12
Adjusted Thyroid Weight (g)[g]			
	0.0195 ± 0.0014 N=11[f]	0.0204 ± 0.0007 N=12	0.0183 ± 0.0008 N=12
Adjusted Liver Weight (g)[g]			
	14.7885 ± 0.6006 N=11[f]	15.0751 ± 0.2601 N=12	15.4710 ± 0.3320 N=12

(continued)

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine Treated F_1 Males (page 3 of 6)

	Atrazine (mg/kg/day, po)		
	0	75	150
Adjusted Paired Adrenal Gland Weight (g)[g]			
	0.0493 ± 0.0033 N=11[f]	0.0502 ± 0.0022 N=12	0.0570 ± 0.0029 N=12
Adjusted Paired Kidney Weight (g)[g]			
	2.5828 ± 0.0744 N=11[f]	2.7595 ± 0.0481 N=12	2.7744 ± 0.0648 N=12
Adjusted Paired Testis Weight (g)[g]			
	2.6125 ± 0.0812 N=11[f]	2.8368 ± 0.0525 N=12	2.9456 ± 0.0707 N=12
Adjusted Paired Epididymis Weight (g)[g]			
	0.4526 ± 0.0189 N=11[f]	0.4522 ± 0.0122 N=12	0.4490 ± 0.0165 N=12
Adjusted Ventral Prostate Weight (g)[g]			
	0.2254 ± 0.0204 N=11[f]	0.2112 ± 0.0132 N=12	0.2097 ± 0.0178 N=12
Adjusted Dorsolateral Prostate Weight (g)[g]			
	0.1652 ± 0.0179 N=11[f]	0.1834 ± 0.0116 N=12	0.1808 ± 0.0156 N=12
Adjusted Prostate Weight (g)[g]			
	0.3907 ± 0.0303 N=11[f]	0.3946 ± 0.0196 N=12	0.3905 ± 0.0264 N=12
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[g]			
	0.5288 ± 0.0418 N=11[f]	0.4572 ± 0.0270 N=12	0.4491 ± 0.0364 N=12
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[g]			
	0.6639 ± 0.0516 N=11[f]	0.6028 ± 0.0333 N=12	0.6040 ± 0.0449 N=12

(continued)

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine Treated F_1 Males (page 4 of 6)

	Atrazine (mg/kg/day, po)		
	0	75	150
Adjusted Pituitary Weight (g)[h]			
	0.0114 ♂♂♂ ± 0.0004 ♂♂♂ N=12	0.0099 ♂ ± 0.0004 N=12	0.0080 ♂♂♂ ± 0.0004 N=12
Adjusted Thyroid Weight (g)[h]			
	0.0185 ± 0.0011 N=12	0.0205 ± 0.0008 N=12	0.0187 ± 0.0007 N=12
Adjusted Liver Weight (g)[h]			
	16.4333 ♦♦♦ ± 0.5017 △△△ N=12	14.7509 ◁◁ ± 0.2801 N=12	14.0254 ◁◁◁ ± 0.3435 N=12
Adjusted Paired Adrenal Gland Weight (g)[h]			
	0.0535 ± 0.0021 N=12	0.0494 ± 0.0021 N=12	0.0539 ± 0.0021 N=12
Adjusted Paired Kidney Weight (g)[h]			
	2.8546 ♂♂ ± 0.0622 ♂♂ N=12	2.7127 ± 0.0624 N=12	2.5458 ♂♂ ± 0.0623 N=12
Adjusted Paired Testis Weight (g)[h]			
	2.7438 ± 0.0445 N=12	2.8015 ± 0.0446 N=12	2.8320 ± 0.0446 N=12
Adjusted Paired Epididymis Weight (g)[h]			
	0.4863 ♂♂♂ ± 0.0105 ♂♂♂ N=12	0.4446 ♂ ± 0.0106 N=12	0.4232 ♂♂♂ ± 0.0106 N=12
Adjusted Ventral Prostate Weight (g)[h]			
	0.2409 ± 0.0128 ♂ N=12	0.2081 ± 0.0129 N=12	0.1977 ± 0.0128 N=12
Adjusted Dorsolateral Prostate Weight (g)[h]			
	0.1975 ± 0.0122 ♂ N=12	0.1789 ± 0.0122 N=12	0.1565 ± 0.0122 N=12

(continued)

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine Treated F_1 Males (page 5 of 6)

	Atrazine (mg/kg/day, po)		
	0	75	150
Adjusted Prostate Weight (g)[h]			
	0.4384 ♂ ± 0.0199 ♂♂ N=12	0.3870 ± 0.0200 N=12	0.3542 ♀ ± 0.0200 N=12
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[h]			
	0.5536 ♂♂ ± 0.0267 ♂♂ N=12	0.4497 ♀ ± 0.0267 N=12	0.4229 ♀♀ ± 0.0267 N=12
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[h]			
	0.7073 ♂♂ ± 0.0314 ♂♂ N=12	0.5904 ♀ ± 0.0315 N=12	0.5646 ♀♀ ± 0.0314 N=12
Thyroxine Hormone (T4) (ug/dL)[e]			
	6.46 ± 0.16 N=12	6.35 ± 0.26 N=12	6.28 ± 0.25 N=12
Thyroid Stimulating Hormone (TSH) (ng/ml)[e]			
	10.95 ± 1.06 N=12	10.89 ± 1.31 N=12	12.66 ± 1.81 N=12

(continued)

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine Treated F_1 Males (page 6 of 6)

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 18 was removed from the study because it was not dosed on the correct postnatal days and male 119 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Males 55, 118 and 127 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Male 54 was found dead on postnatal day 37 after dosing (misdirected dose).
[e]Reported as the mean ± S.E.M.
[f]Decrease in N is due to the body weight for one animal inadvertently not being recorded prior to blood being taken.
[g]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[h]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡ $p<0.05$; ANOVA Test.
‡‡ $p<0.01$; ANOVA Test.
‡‡‡ $p<0.001$; ANOVA Test.
§ $p<0.05$; Test for Linear Trend.
§§ $p<0.01$; Test for Linear Trend.
§§§ $p<0.001$; Test for Linear Trend.
* $p<0.05$; Dunnett's Test.
** $p<0.01$; Dunnett's Test.
*** $p<0.001$; Dunnett's Test.
†† $p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸŸ $p<0.001$; Linear trend test in robust regression model.
Þ $p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model.
ÞÞ $p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
ʊ $p<0.05$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʊʊ $p<0.01$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʊʊʊ $p<0.001$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎ $p<0.05$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎ $p<0.01$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎʎ $p<0.001$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾ $p<0.05$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾ $p<0.01$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾʾ $p<0.001$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
♦♦♦ $p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
△△△ $p<0.001$; Linear trend test in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
◃◃ $p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
◃◃◃ $p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 1 of 6)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
No. of Males on Study	12[a]	14[b]	15
No. of Males at Scheduled Sacrifice	12	13[c]	15
Sacrifice Body Weight (g)[d]			
	316.31 ± 6.46 N=11[e]	316.80 ± 7.41 N=13	311.09 ± 7.88 N=15
Pituitary Weight (g)[d]			
	0.0113 ± 0.0003 N=12	0.0110 ± 0.0005 N=13	0.0116 ± 0.0004 N=14[f]
Thyroid Weight (g)[d]			
#	0.0185 †† ŸŸ ± 0.0012 N=12	0.0220 Þ ± 0.0007 N=13	0.0243 ÞÞ ± 0.0016 N=15
Liver Weight (g)[d]			
	16.4133 ‡‡‡ §§§ ± 0.6404 N=12	22.4886 *** ± 0.6320 N=13	23.8107 *** ± 0.7765 N=15
Paired Adrenal Gland Weight (g)[d]			
	0.0534 ± 0.0025 N=12	0.0536 ± 0.0023 N=12[f]	0.0510 ± 0.0033 N=15
Paired Kidney Weight (g)[d]			
	2.8524 ‡ § ± 0.0865 N=12	3.1923 * ± 0.0776 N=13	3.2025 * ± 0.1025 N=15
Paired Testis Weight (g)[d]			
	2.7402 ± 0.0497 N=12	2.7960 ± 0.0465 N=13	2.7760 ± 0.0604 N=15
Paired Epididymis Weight (g)[d]			
	0.4856 ‡ § ± 0.0129 N=12	0.4670 ± 0.0140 N=13	0.4356 * ± 0.0144 N=15

(continued)

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 2 of 6)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Ventral Prostate Weight (g)[d]			
	0.2407 ± 0.0113 N=12	0.2576 ± 0.0195 N=13	0.2285 ± 0.0159 N=15
Dorsolateral Prostate Weight (g)[d]			
	0.1973 ± 0.0167 N=12	0.2196 ± 0.0122 N=13	0.1954 ± 0.0180 N=15
Prostate Weight (g)[d]			
	0.4380 ± 0.0221 N=12	0.4772 ± 0.0287 N=13	0.4239 ± 0.0232 N=15
Seminal Vesicles with Coagulating Glands Weight (g)[d]			
	0.5529 ± 0.0332 N=12	0.5648 ± 0.0261 N=13	0.4891 ± 0.0348 N=15
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[d]			
	0.7060 ± 0.0259 N=12	0.6814 ± 0.0420 N=13	0.6217 ± 0.0291 N=15
Adjusted Pituitary Weight (g)[g]			
	0.0115 ± 0.0004 N=11[e]	0.0111 ± 0.0004 N=13	0.0116 ± 0.0004 N=14[f]
Adjusted Thyroid Weight (g)[g]			
	0.0190 ♦♦ ± 0.0010 ▵▵ N=11[e]	0.0218 ◃ ± 0.0007 N=13	0.0245 ◃◃ ± 0.0014 N=15
Adjusted Liver Weight (g)[g]			
	16.5695 ☋☋☋ ± 0.5246 ᛤᛤᛤ N=11[e]	22.3261 ❦❦❦ ± 0.4828 N=13	24.0453 ❦❦❦ ± 0.4503 N=15

(continued)

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 3 of 6)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Adjusted Paired Adrenal Gland Weight (g)[g]			
	0.0532 ± 0.0031 N=11[e]	0.0534 ± 0.0030 N=12[f]	0.0513 ± 0.0027 N=15
Adjusted Paired Kidney Weight (g)[g]			
	2.8625 ŬŬŬ ± 0.0616 ĸĸĸ N=11[e]	3.1691 ŷŷ ± 0.0567 N=13	3.2359 ŷŷŷ ± 0.0529 N=15
Adjusted Paired Testis Weight (g)[g]			
	2.7646 ± 0.0504 N=11[e]	2.7878 ± 0.0464 N=13	2.7879 ± 0.0433 N=15
Adjusted Paired Epididymis Weight (g)[g]			
	0.4868 Ŭ ± 0.0145 ĸ N=11[e]	0.4653 ± 0.0133 N=13	0.4381 ŷ ± 0.0124 N=15
Adjusted Ventral Prostate Weight (g)[g]			
	0.2398 ± 0.0165 N=11[e]	0.2553 ± 0.0151 N=13	0.2319 ± 0.0141 N=15
Adjusted Dorsolateral Prostate Weight (g)[g]			
	0.1946 ± 0.0163 N=11[e]	0.2172 ± 0.0150 N=13	0.1988 ± 0.0140 N=15
Adjusted Prostate Weight (g)[g]			
	0.4344 ± 0.0229 N=11[e]	0.4726 ± 0.0211 N=13	0.4306 ± 0.0197 N=15
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[g]			
	0.5620 ± 0.0330 N=11[e]	0.5610 ± 0.0304 N=13	0.4945 ± 0.0284 N=15
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[g]			
	0.7155 ± 0.0328 ĸ N=11[e]	0.6767 ± 0.0302 N=13	0.6285 ± 0.0281 N=15

(continued)

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 4 of 6)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Adjusted Pituitary Weight (g)[h]			
	0.0114 ± 0.0004 N=12	0.0111 ± 0.0004 N=13	0.0115 ± 0.0004 N=14[f]
Adjusted Thyroid Weight (g)[h]			
	0.0186 ♦♦♦ ± 0.0009 △△△ N=12	0.0220 ◁◁ ± 0.0007 N=13	0.0242 ◁◁ ± 0.0013 N=15
Adjusted Liver Weight (g)[h]			
	16.4773 ʊʊʊ ± 0.5775 ʎʎʎ N=12	22.5309 ??? ± 0.5548 N=13	23.7229 ??? ± 0.5167 N=15
Adjusted Paired Adrenal Gland Weight (g)[h]			
	0.0534 ± 0.0030 N=12	0.0536 ± 0.0030 N=12[f]	0.0510 ± 0.0027 N=15
Adjusted Paired Kidney Weight (g)[h]			
	2.8605 ʊʊ ± 0.0768 ʎʎ N=12	3.1976 ?? ± 0.0738 N=13	3.1914 ?? ± 0.0687 N=15
Adjusted Paired Testis Weight (g)[h]			
	2.7444 ± 0.0486 N=12	2.7988 ± 0.0466 N=13	2.7704 ± 0.0434 N=15
Adjusted Paired Epididymis Weight (g)[h]			
	0.4866 ʊ ± 0.0130 ʎʎ N=12	0.4676 ± 0.0125 N=13	0.4342 ?? ± 0.0116 N=15
Adjusted Ventral Prostate Weight (g)[h]			
	0.2415 ± 0.0162 N=12	0.2582 ± 0.0155 N=13	0.2274 ± 0.0145 N=15
Adjusted Dorsolateral Prostate Weight (g)[h]			
	0.1981 ± 0.0163 N=12	0.2201 ± 0.0156 N=13	0.1944 ± 0.0146 N=15

(continued)

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 5 of 6)

	p,p'-Dichlorodiphenyldichloroethylene (mg/kg/day, po)		
	0	50	100
Adjusted Prostate Weight (g)[h]			
	0.4396 ± 0.0238 N=12	0.4783 ± 0.0228 N=13	0.4217 ± 0.0213 N=15
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[h]			
	0.5551 ± 0.0302 N=12	0.5662 ± 0.0290 N=13	0.4861 ± 0.0270 N=15
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[h]			
	0.7086 ± 0.0297 ✗ N=12	0.6830 ± 0.0286 N=13	0.6182 ± 0.0266 N=15
Thyroxine Hormone (T4) (ug/dL)[d]			
	6.46 ‡‡ ± 0.16 §§§ N=12	5.90 ± 0.23 N=13	5.31 ** ± 0.26 N=15
Thyroid Stimulating Hormone (TSH) (ng/ml)[d]			
	10.95 ± 1.06 N=12	14.06 ± 1.58 N=13	14.42 ± 1.81 N=15

(continued)

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the p,p'-Dichlorodiphenyldichloroethylene Treated F_1 Males (page 6 of 6)

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Male 74 was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Male 20 was euthanized on postnatal day 29 after dosing due to a leg injury.
[d]Reported as the mean ± S.E.M.
[e]Decrease in N is due to the body weight for one animal inadvertently not being recorded prior to blood being taken.
[f]Decrease in N is due to one organ weight being a statistical outlier and therefore it was excluded.
[g]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[h]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[††]$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
[ŸŸ]$p<0.01$; Linear trend test in robust regression model.
[Þ]$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model.
[ÞÞ]$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
[‡]$p<0.05$; ANOVA Test.
[‡‡]$p<0.01$; ANOVA Test.
[‡‡‡]$p<0.001$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[§§§]$p<0.001$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.
[**]$p<0.01$; Dunnett's Test.
[***]$p<0.001$; Dunnett's Test.
[♦♦]$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
[♦♦♦]$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
[△△]$p<0.01$; Linear trend test in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
[△△△]$p<0.001$; Linear trend test in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
[◁]$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
[◁◁]$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
[Ʊ]$p<0.05$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ƱƱ]$p<0.01$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ƱƱƱ]$p<0.001$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʎ]$p<0.05$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʎʎ]$p<0.01$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʎʎʎ]$p<0.001$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʾ]$p<0.05$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʾʾ]$p<0.01$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʾʾʾ]$p<0.001$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Vinclozolin Treated F_1 Males (page 1 of 6)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
No. of Males on Study	12[a]	13[b]	12[c]
No. of Males at Scheduled Sacrifice	12	13	12
Sacrifice Body Weight (g)[d]			
#	316.31 ± 6.46 **Ÿ** N=11[e]	321.16 ± 8.86 N=13	302.40 ± 5.64 N=11[e]
Pituitary Weight (g)[d]			
	0.0113 ± 0.0003 N=12	0.0114 ± 0.0004 N=13	0.0108 ± 0.0004 N=12
Thyroid Weight (g)[d]			
#	0.0185 ± 0.0012 N=12	0.0198 ± 0.0007 N=13	0.0205 ± 0.0006 N=12
Liver Weight (g)[d]			
	16.4133 ± 0.6404 N=12	17.6915 ± 0.7660 N=13	17.3103 ± 0.6718 N=12
Paired Adrenal Gland Weight (g)[d]			
	0.0534 ± 0.0025 N=12	0.0577 ± 0.0021 N=13	0.0572 ± 0.0039 N=11[f]
Paired Kidney Weight (g)[d]			
	2.8524 ± 0.0865 N=12	2.9890 ± 0.1054 N=13	2.8058 ± 0.0608 N=12
Paired Testis Weight (g)[d]			
	2.7402 ± 0.0497 N=12	2.9605 ± 0.0688 N=13	2.9348 ± 0.0777 N=12
Paired Epididymis Weight (g)[d]			
	0.4856 **‡‡‡** ± 0.0129 **§§§** N=12	0.4561 ± 0.0144 N=13	0.4001 ******* ± 0.0157 N=12

(continued)

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Vinclozolin Treated F_1 Males (page 2 of 6)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Ventral Prostate Weight (g)[d]			
	0.2407 ‡ ± 0.0113 § N=12	0.2582 ± 0.0169 N=13	0.2064 ± 0.0117 N=12
Dorsolateral Prostate Weight (g)[d]			
	0.1973 ‡‡ ± 0.0167 §§§ N=12	0.1907 ± 0.0136 N=13	0.1298 ** ± 0.0102 N=12
Prostate Weight (g)[d]			
	0.4380 ‡‡ ± 0.0221 §§§ N=12	0.4489 ± 0.0252 N=13	0.3362 ** ± 0.0150 N=12
Seminal Vesicles with Coagulating Glands Weight (g)[d]			
	0.5529 ‡‡‡ ± 0.0332 §§§ N=12	0.4655 ± 0.0355 N=13	0.3044 *** ± 0.0200 N=12
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[d]			
	0.7060 ‡‡ ± 0.0259 §§ N=12	0.6857 ± 0.0441 N=13	0.5443 ** ± 0.0273 N=12
Adjusted Pituitary Weight (g)[g]			
	0.0114 ± 0.0003 N=11[e]	0.0113 ± 0.0003 N=13	0.0112 ± 0.0004 N=11[e]
Adjusted Thyroid Weight (g)[g]			
	0.0191 ± 0.0011 N=11[e]	0.0198 ± 0.0007 N=13	0.0204 ± 0.0007 N=11[e]
Adjusted Liver Weight (g)[g]			
	16.5142 ± 0.4631 N=11[e]	17.1621 ± 0.4613 N=13	17.8317 ± 0.4903 N=11[e]

(continued)

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Vinclozolin Treated F_1 Males (page 3 of 6)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Adjusted Paired Adrenal Gland Weight (g)[g]			
	0.0529 ± 0.0026 N=11[e]	0.0563 ± 0.0016 N=13	0.0598 ± 0.0039 N=10[e,f]
Adjusted Paired Kidney Weight (g)[g]			
	2.8566 ± 0.0556 N=11[e]	2.9193 ± 0.0669 N=13	2.9180 ± 0.0385 N=11[e]
Adjusted Paired Testis Weight (g)[g]			
	2.7618 ♦ ± 0.0425 △ N=11[e]	2.9337 ◁ ± 0.0534 N=13	2.9357 ◁ ± 0.0607 N=11[e]
Adjusted Paired Epididymis Weight (g)[g]			
	0.4848 ♦♦♦ ± 0.0112 △△△ N=11[e]	0.4463 ◁ ± 0.0104 N=13	0.4177 ◁◁◁ ± 0.0127 N=11[e]
Adjusted Ventral Prostate Weight (g)[g]			
	0.2396 ♦ ± 0.0107 N=11[e]	0.2524 ± 0.0127 N=13	0.2100 ± 0.0131 N=11[e]
Adjusted Dorsolateral Prostate Weight (g)[g]			
	0.1944 ♦♦ ± 0.0146 △△ N=11[e]	0.1847 ± 0.0135 N=13	0.1392 ◁◁ ± 0.0116 N=11[e]
Adjusted Prostate Weight (g)[g]			
	0.4340 ♦♦♦ ± 0.0173 △△△ N=11[e]	0.4371 ± 0.0196 N=13	0.3492 ◁◁ ± 0.0183 N=11[e]
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[g]			
	0.5613 ♦♦♦ ± 0.0331 △△△ N=11[e]	0.4551 ◁ ± 0.0307 N=13	0.3188 ◁◁◁ ± 0.0194 N=11[e]
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[g]			
	0.7158 ♦♦♦ ± 0.0234 △△△ N=11[e]	0.6760 ± 0.0424 N=13	0.5504 ◁◁◁ ± 0.0264 N=11[e]

(continued)

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Vinclozolin Treated F_1 Males (page 4 of 6)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Adjusted Pituitary Weight (g)[h]			
	0.0113 ± 0.0004 N=12	0.0114 ± 0.0004 N=13	0.0108 ± 0.0004 N=12
Adjusted Thyroid Weight (g)[h]			
	0.0184 ± 0.0011 N=12	0.0198 ± 0.0008 N=13	0.0205 ± 0.0006 N=12
Adjusted Liver Weight (g)[h]			
	16.3517 ± 0.6436 N=12	17.6998 ± 0.6180 N=13	16.3628 ± 0.6435 N=12
Adjusted Paired Adrenal Gland Weight (g)[h]			
	0.0532 ± 0.0027 N=12	0.0577 ± 0.0026 N=13	0.0574 ± 0.0029 N=11[f]
Adjusted Paired Kidney Weight (g)[h]			
	2.8444 ± 0.0796 N=12	2.9901 ± 0.0765 N=13	2.8126 ± 0.0796 N=12
Adjusted Paired Testis Weight (g)[h]			
	2.7315 ŬŬ ± 0.0512 ƙ N=12	2.9617 ŷŷ ± 0.0491 N=13	2.9422 ŷ ± 0.0512 N=12
Adjusted Paired Epididymis Weight (g)[h]			
	0.4840 ŬŬŬ ± 0.0122 ƙƙƙ N=12	0.4563 ± 0.0117 N=13	0.4015 ŷŷŷ ± 0.0122 N=12
Adjusted Ventral Prostate Weight (g)[h]			
	0.2402 Ŭ ± 0.0139 ƙ N=12	0.2583 ± 0.0134 N=13	0.2068 ± 0.0139 N=12
Adjusted Dorsolateral Prostate Weight (g)[h]			
	0.1969 ŬŬ ± 0.0140 ƙƙƙ N=12	0.1908 ± 0.0134 N=13	0.1301 ŷŷ ± 0.0140 N=12

(continued)

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Vinclozolin Treated F_1 Males (page 5 of 6)

	Vinclozolin (mg/kg/day, po)		
	0	30	100
Adjusted Prostate Weight (g)[h]			
	0.4371 ƱƱ ± 0.0216 ʎʎʎ N=12	0.4491 ± 0.0207 N=13	0.3370 ?? ± 0.0216 N=12
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[h]			
	0.5515 ƱƱƱ ± 0.0307 ʎʎʎ N=12	0.4657 ± 0.0295 N=13	0.3056 ??? ± 0.0307 N=12
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[h]			
	0.7028 ƱƱ ± 0.0309 ʎʎʎ N=12	0.6862 ± 0.0297 N=13	0.5470 ?? ± 0.0309 N=12
Thyroxine Hormone (T4) (ug/dL)[d]			
	6.46 ‡‡‡ ± 0.16 §§§ N=12	4.87 *** ± 0.24 N=13	4.28 *** ± 0.23 N=12
Thyroid Stimulating Hormone (TSH) (ng/ml)[d]			
	10.95 ± 1.06 N=12	10.57 ± 0.62 N=13	12.86 ± 1.16 N=12

(continued)

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Vinclozolin Treated F_1 Males (page 6 of 6)

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 79 and 115 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Males 24, 114 and 131 were removed from the study because their correct postnatal day 0 could not be confirmed.
[d]Reported as the mean ± S.E.M.
[e]Decrease in N is due to the body weight for one animal inadvertently not being recorded prior to blood being taken.
[f]Decrease in N is due to one organ weight being a statistical outlier and therefore it was excluded.
[g]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[h]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[Ÿ]$p<0.05$; Linear trend test in robust regression model.
[‡]$p<0.05$; ANOVA Test.
[‡‡]$p<0.01$; ANOVA Test.
[‡‡‡]$p<0.001$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[§§]$p<0.01$; Test for Linear Trend.
[§§§]$p<0.001$; Test for Linear Trend.
[**]$p<0.01$; Dunnett's Test.
[***]$p<0.001$; Dunnett's Test.
[♦]$p<0.05$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight as covariate. **(17)**
[♦♦]$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight as covariate. **(17)**
[♦♦♦]$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight as covariate. **(17)**
[▵]$p<0.05$; Linear trend test in robust regression model with body weight as covariate. **(17)**
[▵▵]$p<0.01$; Linear trend test in robust regression model with body weight as covariate. **(17)**
[▵▵▵]$p<0.001$; Linear trend test in robust regression model with body weight as covariate. **(17)**
[◃]$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model with body weight as covariate. **(15)**
[◃◃]$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model with body weight as covariate. **(15)**
[◃◃◃]$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model with body weight as covariate. **(15)**
[Ʊ]$p<0.05$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ƱƱ]$p<0.01$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ƱƱƱ]$p<0.001$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʎ]$p<0.05$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʎʎʎ]$p<0.001$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʾ]$p<0.05$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʾʾ]$p<0.01$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
[ʾʾʾ]$p<0.001$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor Treated F_1 Males (page 1 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Males on Study	12[a]	15	13[b]
No. of Males at Scheduled Sacrifice	12	15	13
Sacrifice Body Weight (g)[c]			
	316.31 ± 6.46 N=11[d]	301.97 ± 5.46 N=15	297.66 ± 8.19 N=13
Pituitary Weight (g)[c]			
	0.0113 ± 0.0003 N=12	0.0109 ± 0.0004 N=15	0.0106 ± 0.0003 N=12[e]
Thyroid Weight (g)[c]			
	0.0185 ‡ ± 0.0012 N=12	0.0210 ± 0.0010 N=15	0.0168 ± 0.0009 N=13
Liver Weight (g)[c]			
	16.4133 ± 0.6404 N=12	15.4169 ± 0.5109 N=15	15.1498 ± 0.5405 N=13
Paired Adrenal Gland Weight (g)[c]			
	0.0534 ‡ ± 0.0025 §§ N=12	0.0576 ± 0.0025 N=13[e,f]	0.0647 * ± 0.0035 N=12[f]
Paired Kidney Weight (g)[c]			
	2.8524 ± 0.0865 N=12	2.7784 ± 0.1042 N=15	2.8244 ± 0.1104 N=13
Paired Testis Weight (g)[c]			
	2.7402 ± 0.0470 N=12	2.7707 ± 0.0570 N=15	2.7534 ± 0.0753 N=13
Paired Epididymis Weight (g)[c]			
	0.4856 ± 0.0129 N=12	0.4933 ± 0.0123 N=15	0.4669 ± 0.0169 N=13

(continued)

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor Treated F_1 Males (page 2 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Ventral Prostate Weight (g)[c]			
	0.2407 ± 0.0113 N=12	0.2377 ± 0.0143 N=15	0.2432 ± 0.0149 N=13
Dorsolateral Prostate Weight (g)[c]			
	0.1973 ± 0.0167 N=12	0.1722 ± 0.0119 N=15	0.1719 ± 0.0113 N=13
Prostate Weight (g)[c]			
	0.4380 ± 0.0221 N=12	0.4099 ± 0.0228 N=15	0.4151 ± 0.0219 N=13
Seminal Vesicles with Coagulating Glands Weight (g)[c]			
	0.5529 ‡‡ ± 0.0322 §§ N=12	0.5013 ± 0.0242 N=14[g]	0.4043 ** ± 0.0374 N=13
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[c]			
	0.7060 ± 0.0259 N=12	0.6840 ± 0.0381 N=15	0.6095 ± 0.0370 N=12[h]
Adjusted Pituitary Weight (g)[i]			
	0.0113 ± 0.0004 N=11[d]	0.0109 ± 0.0003 N=15	0.0107 ± 0.0004 N=12[e]
Adjusted Thyroid Weight (g)[i]			
	0.0184 ŬŬ ± 0.0010 N=11[d]	0.0212 ± 0.0008 N=15	0.0172 ± 0.0009 N=13
Adjusted Liver Weight (g)[i]			
	15.8920 ± 0.3471 N=11[d]	15.5956 ± 0.2879 N=15	15.6251 ± 0.3130 N=13

(continued)

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor Treated F_1 Males (page 3 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Adjusted Paired Adrenal Gland Weight (g)[i]			
	0.0505 ƱƱ ± 0.0029 ƛƛƛ N=11[d]	0.0581 ± 0.0025 N=13[e,f]	0.0668 ??? ± 0.0027 N=12[f]
Adjusted Paired Kidney Weight (g)[i]			
	2.7527 ± 0.0837 N=11[d]	2.8068 ± 0.0694 N=15	2.8999 ± 0.0755 N=13
Adjusted Paired Testis Weight (g)[i]			
	2.7131 ± 0.0588 N=11[d]	2.7835 ± 0.0488 N=15	2.7875 ± 0.0531 N=13
Adjusted Paired Epididymis Weight (g)[i]			
	0.4746 ± 0.0139 N=11[d]	0.4963 ± 0.0115 N=15	0.4749 ± 0.0125 N=13
Adjusted Ventral Prostate Weight (g)[i]			
	0.2307 ± 0.0145 N=11[d]	0.2401 ± 0.0120 N=15	0.2496 ± 0.0131 N=13
Adjusted Dorsolateral Prostate Weight (g)[i]			
	0.1857 ± 0.0138 N=11[d]	0.1746 ± 0.0114 N=15	0.1783 ± 0.0124 N=13
Adjusted Prostate Weight (g)[i]			
	0.4164 ± 0.0220 N=11[d]	0.4147 ± 0.0183 N=15	0.4279 ± 0.0199 N=13
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[i]			
	0.5446 Ʊ ± 0.0335 ƛƛ N=11[d]	0.5066 ± 0.0287 N=14[g]	0.4158 ? ± 0.0301 N=13
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[i]			
	0.6935 ± 0.0352 N=11[d]	0.6952 ± 0.0295 N=15	0.6191 ± 0.0329 N=12[h]

(continued)

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor Treated F_1 Males (page 4 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Adjusted Pituitary Weight (g)[j]			
	0.0114 ± 0.0004 N=12	0.0109 ± 0.0003 N=15	0.0106 ± 0.0004 N=12[e]
Adjusted Thyroid Weight (g)[j]			
	0.0186 ŏŏ ± 0.0009 N=12	0.0209 ± 0.0008 N=15	0.0169 ± 0.0009 N=13
Adjusted Liver Weight (g)[j]			
	16.5011 ± 0.4156 ĸ N=12	15.3167 ± 0.3719 N=15	15.1843 ± 0.3991 N=13
Adjusted Paired Adrenal Gland Weight (g)[j]			
	0.0536 ŏ ± 0.0026 ĸĸ N=12	0.0571 ± 0.0025 N=13[e,f]	0.0650 ŏŏ ± 0.0026 N=14[f]
Adjusted Paired Kidney Weight (g)[j]			
	2.8657 ± 0.0879 N=12	2.7633 ± 0.0786 N=15	2.8296 ± 0.0844 N=13
Adjusted Paired Testis Weight (g)[j]			
	2.7483 ± 0.0530 N=12	2.7614 ± 0.0474 N=15	2.7565 ± 0.0509 N=13
Adjusted Paired Epididymis Weight (g)[j]			
	0.4875 ± 0.0119 N=12	0.4911 ± 0.0106 N=15	0.4677 ± 0.0114 N=13
Adjusted Ventral Prostate Weight (g)[j]			
	0.2423 ± 0.0124 N=12	0.2358 ± 0.0111 N=15	0.2438 ± 0.0119 N=13
Adjusted Dorsolateral Prostate Weight (g)[j]			
	0.1985 ± 0.0129 N=12	0.1709 ± 0.0116 N=15	0.1724 ± 0.0124 N=13

(continued)

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor Treated F_1 Males (page 5 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Adjusted Prostate Weight (g)[j]			
	0.4408 ± 0.0196 N=12	0.4067 ± 0.0175 N=15	0.4162 ± 0.0188 N=13
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[j]			
	0.5543 ♂♂ ± 0.0322 ♂♂ N=12	0.4998 ± 0.0298 N=14[g]	0.4046 ♀♀ ± 0.0309 N=13
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[j]			
	0.7148 ± 0.0332 ♂ N=12	0.6845 ± 0.0296 N=15	0.6001 ± 0.0332 N=12[h]
Thyroxine Hormone (T4) (ug/dL)[c]			
	6.46 ± 0.16 N=12	6.11 ± 0.24 N=15	6.66 ± 0.25 N=13
Thyroid Stimulating Hormone (TSH) (ng/ml)[c]			
	10.95 ± 1.06 N=12	10.98 ± 1.65 N=15	10.84 ± 0.74 N=13

(continued)

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor Treated F_1 Males (page 6 of 6)

[a]Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Males 17 and 30 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c]Reported as the mean ± S.E.M.
[d]Decrease in N is due to the body weight for one animal inadvertently not being recorded prior to blood being taken.
[e]Decrease in N is due to one organ weight being a statistical outlier and therefore it was excluded.
[f]Decrease in N is due to one adrenal gland from one animal inadvertently being lost prior to weighing.
[g]Decrease in N is due to one seminal vesicles with coagulating glands inadvertently being nicked and leaking prior to weighing and therefore the weight was excluded.
[h]Decrease in N is due to one levator ani plus bulbcavernosus muscle complex inadvertently not being completely removed from the animal and therefore the weight was excluded.
[i]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[j]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
‡p<0.05; ANOVA Test.
‡‡p<0.01; ANOVA Test.
§§p<0.01; Test for Linear Trend.
*p<0.05; Dunnett's Test.
**p<0.01; Dunnett's Test.
ʊp<0.05; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʊʊp<0.01; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎp<0.05; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎp<0.01; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎʎp<0.001; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ϑp<0.05; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ϑϑp<0.01; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ϑϑϑp<0.001; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil Treated F_1 Males (page 1 of 6)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Males on Study	15	15	15
No. of Males at Scheduled Sacrifice	14[a]	15	14[b]
Sacrifice Body Weight (g)[c]			
	320.70 ‡‡‡ ± 6.74 §§§ N=14	294.04 ** ± 7.18 N=15	173.91 *** ± 3.95 N=13[d]
Pituitary Weight (g)[c]			
	0.0117 ‡‡ ± 0.0006 §§ N=14	0.0116 ± 0.0003 N=14[e]	0.0096 ** ± 0.0005 N=14
Thyroid Weight (g)[c]			
	0.0273 ‡‡‡ ± 0.0011 §§§ N=14	0.0770 *** ± 0.0044 N=15	0.0886 *** ± 0.0067 N=14
Liver Weight (g)[c]			
	17.6196 ‡‡‡ ± 0.5792 §§§ N=14	15.2176 ** ± 0.6546 N=15	7.7000 *** ± 0.3260 N=14
Paired Adrenal Gland Weight (g)[c]			
	0.0480 ‡‡‡ ± 0.0016 §§§ N=14	0.0385 *** ± 0.0014 N=15	0.0254 *** ± 0.0011 N=14
Paired Kidney Weight (g)[c]			
	3.1147 ‡‡‡ ± 0.0800 §§§ N=14	2.4769 *** ± 0.0858 N=15	1.4226 *** ± 0.0411 N=14
Paired Testis Weight (g)[c]			
	2.8678 ‡‡ ± 0.0299 §§ N=14	2.8014 ± 0.0447 N=15	2.6496 ** ± 0.0539 N=14
Paired Epididymis Weight (g)[c]			
	0.4564 ‡‡ ± 0.0142 §§§ N=14	0.4386 ± 0.0160 N=15	0.3791 ** ± 0.0138 N=14

(continued)

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil Treated F_1 Males (page 2 of 6)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Ventral Prostate Weight (g)[c]			
	0.2657 ‡‡ ± 0.0168 §§ N=14	0.2410 ± 0.0147 N=15	0.1888 ** ± 0.0157 N=14
Dorsolateral Prostate Weight (g)[c]			
	0.1852 ‡ ± 0.0130 §§ N=14	0.1692 ± 0.0125 N=15	0.1310 ** ± 0.0113 N=14
Prostate Weight (g)[c]			
	0.4509 ‡‡ ± 0.0258 §§§ N=14	0.4101 ± 0.0223 N=15	0.3199 *** ± 0.0207 N=14
Seminal Vesicles with Coagulating Glands Weight (g)[c]			
	0.6396 ‡ ± 0.0462 § N=13[f]	0.6910 ± 0.0431 N=15	0.5244 ± 0.0372 N=14
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[c]			
	0.6384 ‡‡‡ ± 0.0279 §§§ N=14	0.6539 ± 0.0326 N=15	0.3702 *** ± 0.0308 N=14
Adjusted Pituitary Weight (g)[g]			
	0.0106 ± 0.0008 N=14	0.0111 ± 0.0006 N=14[e]	0.0115 ± 0.0012 N=13[d]
Adjusted Thyroid Weight (g)[g]			
	0.0140 ŬŬŬ ± 0.0071 N=14	0.0701 *** ± 0.0050 N=15	0.1076 *** ± 0.0106 N=13[d]
Adjusted Liver Weight (g)[g]			
	13.2806 Ŭ ± 0.4405 ƛ N=14	12.9385 ± 0.3085 N=15	15.0343 ± 0.6553 N=13[d]

(continued)

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil Treated F_1 Males (page 3 of 6)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Adjusted Paired Adrenal Gland Weight (g)[g]			
	0.0437 ♂♂ ± 0.0023 N=14	0.0363 ♀♀ ± 0.0016 N=15	0.0324 ± 0.0034 N=13[d]
Adjusted Paired Kidney Weight (g)[g]			
	2.6024 ♂♂♂ ± 0.0769 N=14	2.2132 ♀♀♀ ± 0.0539 N=15	2.3002 ± 0.1145 N=13[d]
Adjusted Paired Testis Weight (g)[g]			
	2.7938 ± 0.0706 N=14	2.7633 ± 0.0495 N=15	2.8045 ± 0.1051 N=13[d]
Adjusted Paired Epididymis Weight (g)[g]			
	0.3881 ± 0.0224 ♂ N=14	0.4035 ± 0.0157 N=15	0.4958 ± 0.0334 N=13[d]
Adjusted Ventral Prostate Weight (g)[g]			
	0.2045 ± 0.0253 N=14	0.2094 ± 0.0177 N=15	0.2924 ± 0.0376 N=13[d]
Adjusted Dorsolateral Prostate Weight (g)[g]			
	0.1597 ± 0.0213 N=14	0.1560 ± 0.0149 N=15	0.1753 ± 0.0317 N=13[d]
Adjusted Prostate Weight (g)[g]			
	0.3641 ± 0.0372 N=14	0.3654 ± 0.0261 N=15	0.4677 ± 0.0554 N=13[d]
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[g]			
	0.4696 ♂ ± 0.0640 N=13[f]	0.6022 ♀ ± 0.0441 N=15	0.8212 ♀ ± 0.0912 N=13[d]
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[g]			
	0.5227 ± 0.0495 N=14	0.5943 ± 0.0347 N=15	0.5669 ± 0.0737 N=13[d]

(continued)

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil Treated F_1 Males (page 4 of 6)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Adjusted Pituitary Weight (g)[h]			
	0.0116 ŬŬ ± 0.0005 ĸĸ N=14	0.0117 ± 0.0005 N=14[e]	0.0097 ŷŷ ± 0.0005 N=14
Adjusted Thyroid Weight (g)[h]			
	0.0273 ŬŬŬ ± 0.0048 ĸĸĸ N=14	0.0770 ŷŷŷ ± 0.0046 N=15	0.0885 ŷŷŷ ± 0.0048 N=14
Adjusted Liver Weight (g)[h]			
	17.5770 ŬŬŬ ± 0.5076 ĸĸĸ N=14	15.2090 ŷŷ ± 0.4901 N=15	7.7519 ŷŷŷ ± 0.5077 N=14
Adjusted Paired Adrenal Gland Weight (g)[h]			
	0.0479 ŬŬŬ ± 0.0014 ĸĸĸ N=14	0.0385 ŷŷŷ ± 0.0013 N=15	0.0255 ŷŷŷ ± 0.0014 N=14
Adjusted Paired Kidney Weight (g)[h]			
	3.1088 ŬŬŬ ± 0.0671 ĸĸĸ N=14	2.4757 ŷŷŷ ± 0.0648 N=15	1.4297 ŷŷŷ ± 0.0672 N=14
Adjusted Paired Testis Weight (g)[h]			
	2.8640 ŬŬ ± 0.0400 ĸĸĸ N=14	2.8007 ± 0.0386 N=15	2.6542 ŷŷ ± 0.0400 N=14
Adjusted Paired Epididymis Weight (g)[h]			
	0.4550 ŬŬŬ ± 0.0130 ĸĸĸ N=14	0.4383 ± 0.0126 N=15	0.3808 ŷŷŷ ± 0.0130 N=14
Adjusted Ventral Prostate Weight (g)[h]			
	0.2646 ŬŬ ± 0.0149 ĸĸ N=14	0.2407 ± 0.0143 N=15	0.1902 ŷŷ ± 0.0149 N=14
Adjusted Dorsolateral Prostate Weight (g)[h]			
	0.1848 Ŭ ± 0.0124 ĸĸ N=14	0.1691 ± 0.0120 N=15	0.1315 ŷŷ ± 0.0124 N=14

(continued)

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil Treated F_1 Males (page 5 of 6)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Adjusted Prostate Weight (g)[h]			
	0.4494 ƱƱƱ ± 0.0221 ʎʎʎ N=14	0.4098 ± 0.0213 N=15	0.3217 ??? ± 0.0221 N=14
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[h]			
	0.6358 Ʊ ± 0.0404 ʎʎ N=13[f]	0.6905 ± 0.0376 N=15	0.5285 ± 0.0390 N=14
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[h]			
	0.6367 ƱƱƱ ± 0.0300 ʎʎʎ N=14	0.6535 ± 0.0290 N=15	0.3722 ??? ± 0.0300 N=14
Thyroxine Hormone (T4) (ug/dL)[c]			
#	5.78 ††† ± 0.27 ŸŸŸ N=14	0.53 ÞÞÞ ± 0.08 N=9[i]	0.37 ÞÞÞ ± 0.01 N=6[i]
Thyroid Stimulating Hormone (TSH) (ng/ml)[c]			
#	11.54 ††† ± 0.90 ŸŸŸ N=14	82.13 ÞÞÞ ± 4.60 N=15	134.63 ÞÞÞ ± 7.89 N=14

(continued)

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil Treated F_1 Males (page 6 of 6)

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Male 268 was found dead on postnatal day 50 prior to dosing.
[c]Reported as the mean ± S.E.M.
[d]Decrease in N is due to one sacrifice weight inadvertently not being recorded.
[e]Decrease in N is due to one organ weight being a statistical outlier and therefore it was excluded.
[f]Decrease in N is due to one seminal vesicles with coagulating glands inadvertently being nicked and leaking prior to weighing and therefore the weight was excluded.
[g]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[h]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
[i]Decrease in N is due to one or more thyroxine values being below the minimum detection limit of the assay and they were therefore excluded.
‡p<0.05; ANOVA Test.
‡‡p<0.01; ANOVA Test.
‡‡‡p<0.001; ANOVA Test.
§p<0.05; Test for Linear Trend.
§§p<0.01; Test for Linear Trend.
§§§p<0.001; Test for Linear Trend.
**p<0.01; Dunnett's Test.
***p<0.001; Dunnett's Test.
ʊp<0.05; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʊʊp<0.01; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʊʊʊp<0.001; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎp<0.05; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎp<0.01; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎʎp<0.001; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾp<0.05; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾp<0.01; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾʾp<0.001; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
†††p<0.001; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸŸp<0.001; Linear trend test in robust regression model.
ÞÞÞp<0.001; Individual t-test for pairwise comparisons to control in robust regression model.

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole Treated F_1 Males (page 1 of 6)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
No. of Males at Scheduled Sacrifice	14[a]	15	14[b]
Sacrifice Body Weight (g)[c]	320.70 ± 6.74 N=14	315.68 ± 6.57 N=15	301.50 ± 7.51 N=14
Pituitary Weight (g)[c]	0.0117 ± 0.0006 N=14	0.0107 ± 0.0004 N=15	0.0117 ± 0.0005 N=14
Thyroid Weight (g)[c]	0.0273 ± 0.0011 N=14	0.0266 ± 0.0011 N=15	0.0267 ± 0.0006 N=14
Liver Weight (g)[c]	17.6196 ± 0.5792 N=14	19.1954 ± 0.5408 N=15	19.1401 ± 0.8105 N=14
Paired Adrenal Gland Weight (g)[c]			
#	0.0480 ††† ± 0.0016 ŸŸŸ N=14	0.0704 ÞÞÞ ± 0.0036 N=15	0.0908 ÞÞÞ ± 0.0047 N=14
Paired Kidney Weight (g)[c]	3.1147 ± 0.0800 N=14	3.1021 ± 0.0708 N=15	3.1597 ± 0.1181 N=14
Paired Testis Weight (g)[c]			
#	2.8678 ††† ± 0.0299 ŸŸŸ N=14	2.8051 ± 0.0563 N=15	2.7212 ÞÞÞ ± 0.0223 N=14
Paired Epididymis Weight (g)[c]	0.4564 ± 0.0142 § N=14	0.4294 ± 0.0139 N=15	0.4118 ± 0.0109 N=14

(continued)

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole Treated F_1 Males (page 2 of 6)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Ventral Prostate Weight (g)[c]			
#	0.2657 ± 0.0168 Ÿ N=14	0.2372 ± 0.0116 N=15	0.2058 ± 0.0243 N=14
Dorsolateral Prostate Weight (g)[c]			
	0.1852 ± 0.0130 N=14	0.1572 ± 0.0143 N=15	0.1476 ± 0.0126 N=14
Prostate Weight (g)[c]			
	0.4509 ± 0.0258 § N=14	0.3944 ± 0.0237 N=15	0.3534 ± 0.0324 N=14
Seminal Vesicles with Coagulating Glands Weight (g)[c]			
	0.6396 ‡‡‡ ± 0.0462 §§§ N=13[d]	0.4789 ** ± 0.0215 N=15	0.4193 *** ± 0.0372 N=14
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[c]			
	0.6384 ± 0.0279 § N=14	0.5757 ± 0.0262 N=15	0.5425 ± 0.0306 N=14
Adjusted Pituitary Weight (g)[e]			
	0.0114 ± 0.0005 N=14	0.0106 ± 0.0004 N=15	0.0120 ± 0.0005 N=14
Adjusted Thyroid Weight (g)[e]			
	0.0271 ± 0.0010 N=14	0.0265 ± 0.0010 N=15	0.0270 ± 0.0010 N=14
Adjusted Liver Weight (g)[e]			
	16.9686 ƱƱƱ ± 0.3347 ƛƛƛ N=14	18.9523 ??? ± 0.3190 N=15	20.0516 ??? ± 0.3397 N=14

(continued)

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole Treated F_1 Males (page 3 of 6)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Adjusted Paired Adrenal Gland Weight (g)[e]	0.0464 ♦♦♦ ± 0.0020 △△△ N=14	0.0698 ◁◁◁ ± 0.0029 N=15	0.0930 ◁◁◁ ± 0.0042 N=14
Adjusted Paired Kidney Weight (g)[e]	3.0337 ℧ ± 0.0604 ✗ N=14	3.0718 ± 0.0575 N=15	3.2730 ☮ ± 0.0613 N=14
Adjusted Paired Testis Weight (g)[e]	2.8591 ♦♦ ± 0.0287 △△ N=14	2.8019 ± 0.0537 N=15	2.7334 ◁◁ ± 0.0238 N=14
Adjusted Paired Epididymis Weight (g)[e]	0.4505 ± 0.0126 N=14	0.4272 ± 0.0120 N=15	0.4201 ± 0.0128 N=14
Adjusted Ventral Prostate Weight (g)[e]	0.2616 ± 0.0162 N=14	0.2356 ± 0.0109 N=15	0.2117 ± 0.0231 N=14
Adjusted Dorsolateral Prostate Weight (g)[e]	0.1817 ± 0.0135 N=14	0.1559 ± 0.0129 N=15	0.1525 ± 0.0137 N=14
Adjusted Prostate Weight (g)[e]	0.4432 ± 0.0277 N=14	0.3915 ± 0.0264 N=15	0.3642 ± 0.0281 N=14
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[e]	0.6282 ℧℧ ± 0.0363 ✗✗✗ N=13[d]	0.4747 ☮☮ ± 0.0334 N=15	0.4344 ☮☮ ± 0.0355 N=14
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[e]	0.6287 ± 0.0280 N=14	0.5721 ± 0.0267 N=15	0.5561 ± 0.0285 N=14

(continued)

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole Treated F_1 Males (page 4 of 6)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Adjusted Pituitary Weight (g)[f]			
	0.0116 ± 0.0005 N=14	0.0107 ± 0.0005 N=15	0.0118 ± 0.0005 N=14
Adjusted Thyroid Weight (g)[f]			
	0.0273 ± 0.0010 N=14	0.0265 ± 0.0010 N=15	0.0268 ± 0.0010 N=14
Adjusted Liver Weight (g)[f]			
	17.5861 ± 0.5568 ✗ N=14	19.1172 ± 0.5382 N=15	19.2573 ± 0.5575 N=14
Adjusted Paired Adrenal Gland Weight (g)[f]			
	0.0478 ♦♦♦ ± 0.0021 △△△ N=14	0.0701 ◁◁◁ ± 0.0029 N=15	0.0913 ◁◁◁ ± 0.0041 N=14
Adjusted Paired Kidney Weight (g)[f]			
	3.1101 ± 0.0791 N=14	3.0915 ± 0.0765 N=15	3.1756 ± 0.0792 N=14
Adjusted Paired Testis Weight (g)[f]			
	2.8673 ♦♦♦ ± 0.0285 △△△ N=14	2.8038 ± 0.0542 N=15	2.7232 ◁◁◁ ± 0.0216 N=14
Adjusted Paired Epididymis Weight (g)[f]			
	0.4559 ± 0.0125 ✗ N=14	0.4284 ± 0.0121 N=15	0.4134 ± 0.0125 N=14
Adjusted Ventral Prostate Weight (g)[f]			
	0.2652 ± 0.0143 △ N=14	0.2359 ± 0.0122 N=15	0.2078 ± 0.0222 N=14
Adjusted Dorsolateral Prostate Weight (g)[f]			
	0.1849 ± 0.0133 N=14	0.1565 ± 0.0128 N=15	0.1486 ± 0.0133 N=14

(continued)

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole Treated F_1 Males (page 5 of 6)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Adjusted Prostate Weight (g)[f]			
	0.4501 ± 0.0265 ✗ N=14	0.3924 ± 0.0256 N=15	0.3564 ± 0.0265 N=14
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[f]			
	0.6389 ʊʊʊ ± 0.0367 ✗✗✗ N=13[d]	0.4777 ♀♀ ± 0.0341 N=15	0.4212 ♀♀♀ ± 0.0354 N=14
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[f]			
	0.6377 ± 0.0280 ✗ N=14	0.5742 ± 0.0270 N=15	0.5448 ± 0.0280 N=14
Thyroxine Hormone (T4) (ug/dL)[c]			
	5.78 ± 0.27 N=14	5.58 ± 0.21 N=15	5.65 ± 0.20 N=14
Thyroid Stimulating Hormone (TSH) (ng/ml)[c]			
	11.54 ± 0.90 N=14	10.02 ± 0.64 N=15	11.15 ± 0.88 N=14

(continued)

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole Treated F_1 Males (page 6 of 6)

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Male 242 was found dead on postnatal day 37 prior to dosing (misdirected dose).
[c]Reported as the mean ± S.E.M.
[d]Decrease in N is due to one seminal vesicles with coagulating glands inadvertently being nicked and leaking prior to weighing and therefore the weight was excluded.
[e]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[f]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
†††$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
Ÿ$p\leq0.05$; Linear trend test in robust regression model.
ŸŸŸ$p<0.001$; Linear trend test in robust regression model.
ÞÞÞ$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.
‡‡‡$p<0.001$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§§$p<0.001$; Test for Linear Trend.
**$p<0.01$; Dunnett's Test.
***$p<0.001$; Dunnett's Test.
Ʊ$p<0.05$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ƱƱ$p<0.01$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ƱƱƱ$p<0.001$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎ$p<0.05$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎʎ$p<0.001$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾ$p<0.05$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾ$p<0.01$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾʾ$p<0.001$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
♦♦$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
♦♦♦$p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
∆$p<0.05$; Linear trend test in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
∆∆$p<0.01$; Linear trend test in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
∆∆∆$p<0.001$; Linear trend test in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
◃◃$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
◃◃◃$p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.

Table 7-G. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Linuron Treated F_1 Males (page 1 of 6)

	Linuron (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
No. of Males at Scheduled Sacrifice	14[a]	15	15
Sacrifice Body Weight (g)[b]			
	320.70 ‡‡‡ ± 6.74 §§§ N=14	298.66 * ± 5.69 N=15	268.89 *** ± 6.87 N=15
Pituitary Weight (g)[b]			
	0.0117 ‡‡‡ ± 0.0006 §§§ N=14	0.0097 ** ± 0.0003 N=15	0.0092 *** ± 0.0003 N=15
Thyroid Weight (g)[b]			
	0.0273 ‡‡ ± 0.0011 § N=14	0.0294 ± 0.0009 N=15	0.0242 * ± 0.0008 N=15
Liver Weight (g)[b]			
	17.6196 ‡‡ ± 0.5792 §§ N=14	16.8580 ± 0.6195 N=15	14.9885 ** ± 0.5601 N=15
Paired Adrenal Gland Weight (g)[b]			
	0.0480 ± 0.0016 N=14	0.0483 ± 0.0016 N=15	0.0464 ± 0.0025 N=15
Paired Kidney Weight (g)[b]			
#	3.1147 † ± 0.0800 ŸŸ N=14	2.9232 Þ ± 0.0549 N=15	2.7279 ÞÞ ± 0.1179 N=15
Paired Testis Weight (g)[b]			
	2.8678 ‡ ± 0.0299 §§ N=14	2.7752 ± 0.0454 N=15	2.6670 ** ± 0.0552 N=15
Paired Epididymis Weight (g)[b]			
	0.4564 ‡‡ ± 0.0142 §§§ N=14	0.4186 ± 0.0134 N=15	0.3809 *** ± 0.0135 N=15

(continued)

Table 7-G. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Linuron Treated F_1 Males (page 2 of 6)

	Linuron (mg/kg/day, po)		
	0	50	100
Ventral Prostate Weight (g)[b]			
	0.2657 ‡‡‡ ± 0.0168 §§§ N=14	0.1943 ** ± 0.0090 N=14[c]	0.1845 *** ± 0.0143 N=15
Dorsolateral Prostate Weight (g)[b]			
	0.1852 ‡‡ ± 0.0130 §§ N=14	0.1466 * ± 0.0117 N=15	0.1275 ** ± 0.0103 N=15
Prostate Weight (g)[b]			
	0.4509 ‡‡‡ ± 0.0258 §§§ N=14	0.3343 *** ± 0.0129 N=14[d]	0.3120 *** ± 0.0210 N=15
Seminal Vesicles with Coagulating Glands Weight (g)[b]			
	0.6396 ‡‡‡ ± 0.0462 §§§ N=13[e]	0.4660 ** ± 0.0344 N=15	0.3549 *** ± 0.0370 N=14[e]
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[b]			
	0.6384 ‡‡‡ ± 0.0279 §§§ N=14	0.5437 * ± 0.0320 N=15	0.4559 *** ± 0.0224 N=15
Adjusted Pituitary Weight (g)[f]			
	0.0109 ± 0.0005 N=14	0.0096 ± 0.0004 N=15	0.0100 ± 0.0005 N=15
Adjusted Thyroid Weight (g)[f]			
	0.0268 ʊ ± 0.0011 N=14	0.0293 ± 0.0009 N=15	0.0248 ± 0.0011 N=15
Adjusted Liver Weight (g)[f]			
	15.6059 ʊ ± 0.3403 ʎʎ N=14	16.6074 ʔ* ± 0.2832 N=15	17.1187 ʔ* ± 0.3373 N=15

(continued)

Table 7-G. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Linuron Treated F_1 Males (page 3 of 6)

	Linuron (mg/kg/day, po)		
	0	50	100
Adjusted Paired Adrenal Gland Weight (g)[f]			
	0.0462 ± 0.0023 N=14	0.0481 ± 0.0019 N=15	0.0483 ± 0.0023 N=15
Adjusted Paired Kidney Weight (g)[f]			
	2.8363 ± 0.0549 N=14	2.8885 ± 0.0505 N=15	3.0223 ± 0.0707 N=15
Adjusted Paired Testis Weight (g)[f]			
	2.8254 ± 0.0531 N=14	2.7699 ± 0.0442 N=15	2.7118 ± 0.0526 N=15
Adjusted Paired Epididymis Weight (g)[f]			
	0.4372 ± 0.0154 N=14	0.4162 ± 0.0128 N=15	0.4011 ± 0.0153 N=15
Adjusted Ventral Prostate Weight (g)[f]			
	0.2501 ♂ ± 0.0157 N=14	0.1925 ♀* ± 0.0135 N=14[c]	0.2008 ± 0.0155 N=15
Adjusted Dorsolateral Prostate Weight (g)[f]			
	0.1653 ± 0.0126 N=14	0.1441 ± 0.0105 N=15	0.1486 ± 0.0125 N=15
Adjusted Prostate Weight (g)[f]			
	0.4157 ♂ ± 0.0222 N=14	0.3302 ♀♀* ± 0.0190 N=14[d]	0.3487 ± 0.0219 N=15
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[f]			
	0.5873 ♂ ± 0.0442 ✗ N=13[e]	0.4618 ± 0.0357 N=15	0.4081 ♀* ± 0.0432 N=14[e]
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[f]			
	0.5780 ± 0.0277 N=14	0.5362 ± 0.0231 N=15	0.5199 ± 0.0275 N=15

(continued)

Table 7-G. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Linuron Treated F_1 Males (page 4 of 6)

	Linuron (mg/kg/day, po)		
	0	50	100
Adjusted Pituitary Weight (g)[g]			
	0.0117 ♂♂♂ ± 0.0004 ♂♂♂ N=14	0.0097 ♀♀ ± 0.0004 N=15	0.0092 ♀♀♀ ± 0.0004 N=15
Adjusted Thyroid Weight (g)[g]			
	0.0273 ♂♂ ± 0.0010 ♂ N=14	0.0294 ± 0.0009 N=15	0.0242 ♀ ± 0.0009 N=15
Adjusted Liver Weight (g)[g]			
	17.6360 ♂♂ ± 0.5489 ♂♂ N=14	16.8589 ± 0.5303 N=15	14.9724 ♀♀ ± 0.5303 N=15
Adjusted Paired Adrenal Gland Weight (g)[g]			
	0.0480 ± 0.0020 N=14	0.0483 ± 0.0019 N=15	0.0464 ± 0.0019 N=15
Adjusted Paired Kidney Weight (g)[g]			
	3.1172 ♦♦ ± 0.0768 △△ N=14	2.9233 ◁ ± 0.0457 N=15	2.7254 ◁◁ ± 0.1004 N=15
Adjusted Paired Testis Weight (g)[g]			
	2.8687 ♂♂ ± 0.0449 ♂♂ N=14	2.7752 ± 0.0434 N=15	2.6662 ♀♀ ± 0.0434 N=15
Adjusted Paired Epididymis Weight (g)[g]			
	0.4567 ♂♂♂ ± 0.0134 ♂♂♂ N=14	0.4186 ± 0.0129 N=15	0.3806 ♀♀♀ ± 0.0129 N=15
Adjusted Ventral Prostate Weight (g)[g]			
	0.2662 ♂♂♂ ± 0.0129 ♂♂♂ N=14	0.1941 ♀♀♀ ± 0.0129 N=14[c]	0.1843 ♀♀♀ ± 0.0124 N=15
Adjusted Dorsolateral Prostate Weight (g)[g]			
	0.1854 ♂♂ ± 0.0117 ♂♂♂ N=14	0.1466 ♀ ± 0.0113 N=15	0.1273 ♀♀ ± 0.0113 N=15

(continued)

Table 7-G. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Linuron Treated F_1 Males (page 5 of 6)

	Linuron (mg/kg/day, po)		
	0	50	100
Adjusted Prostate Weight (g)[g]			
	0.4516 ƱƱƱ ± 0.0192 ʎʎʎ N=14	0.3340 ƾƾƾ ± 0.0192 N=14[d]	0.3116 ƾƾƾ ± 0.0186 N=15
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[g]			
	0.6398 ƱƱƱ ± 0.0402 ʎʎʎ N=13[e]	0.4661 ƾƾ ± 0.0374 N=15	0.3547 ƾƾƾ ± 0.0387 N=14[e]
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[g]			
	0.6393 ƱƱƱ ± 0.0249 ʎʎʎ N=14	0.5437 ƾ ± 0.0240 N=15	0.4551 ƾƾƾ ± 0.0240 N=15
Thyroxine Hormone (T4) (ug/dL)[b]			
	5.78 ‡‡‡ ± 0.27 §§§ N=14	4.60 ** ± 0.30 N=14	3.40 *** ± 0.15 N=15
Thyroid Stimulating Hormone (TSH) (ng/ml)[b]			
	11.54 ‡ ± 0.90 N=14	8.98 * ± 0.52 N=14	9.49 ± 0.74 N=15

(continued)

Table 7-G. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Linuron Treated F_1 Males (page 6 of 6)

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Reported as the mean ± S.E.M.
[c]Decrease in N is due to one organ weight being a statistical outlier and therefore it was excluded.
[d]Decrease in N is due to one ventral prostate weight being a statistical outlier and therefore the total prostate weight could not be calculated.
[e]Decrease in N is due to one seminal vesicles with coagulating glands inadvertently being nicked and leaking prior to weighing and therefore the weight was excluded.
[f]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[g]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
[#]Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
‡$p<0.05$; ANOVA Test.
‡‡$p<0.01$; ANOVA Test.
‡‡‡$p<0.001$; ANOVA Test.
§$p<0.05$; Test for Linear Trend.
§§$p<0.01$; Test for Linear Trend.
§§§$p<0.001$; Test for Linear Trend.
*$p<0.05$; Dunnett's Test.
**$p<0.01$; Dunnett's Test.
***$p<0.001$; Dunnett's Test.
†$p<0.05$; Wald Chi-square Test for overall treatment effect in robust regression model.
ŸŸ$p<0.01$; Linear trend test in robust regression model.
Þ$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model.
ÞÞ$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
Ʊ$p<0.05$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ƱƱ$p<0.01$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ƱƱƱ$p<0.001$; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎ$p<0.05$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎ$p<0.01$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎʎ$p<0.001$; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾ$p<0.05$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾ$p<0.01$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
ʾʾʾ$p<0.001$; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
♦♦$p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
△△$p<0.01$; Linear trend test in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
◃$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.
◃◃$p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model with body weight at sacrifice or on postnatal day 21 as covariate.

Table 7-H. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Phenobarbital Treated F_1 Males (page 1 of 6)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
No. of Males on Study	15	15	15
No. of Males at Scheduled Sacrifice	14[a]	15	15
Sacrifice Body Weight (g)[b]			
	320.70 ± 6.74 § N=14	312.07 ± 7.63 N=15	296.96 ± 7.23 N=15
Pituitary Weight (g)[b]			
	0.0117 ± 0.0006 N=14	0.0105 ± 0.0006 N=14[c]	0.0104 ± 0.0002 N=13[c]
Thyroid Weight (g)[b]			
	0.0273 ‡ ± 0.0011 §§ N=14	0.0319 * ± 0.0014 N=15	0.0325 * ± 0.0014 N=15
Liver Weight (g)[b]			
	17.6196 ‡‡‡ ± 0.5792 §§§ N=14	20.3434 * ± 0.6582 N=15	21.8401 *** ± 0.7753 N=15
Paired Adrenal Gland Weight (g)[b]			
	0.0480 ± 0.0016 N=14	0.0529 ± 0.0024 N=15	0.0483 ± 0.0028 N=15
Paired Kidney Weight (g)[b]			
	3.1147 ± 0.0800 N=14	3.0568 ± 0.0934 N=15	2.9835 ± 0.0821 N=15
Paired Testis Weight (g)[b]			
	2.8678 ‡‡ ± 0.0299 §§ N=14	2.7704 ± 0.0438 N=15	2.6432 ** ± 0.0580 N=15
Paired Epididymis Weight (g)[b]			
	0.4564 ‡ ± 0.0142 §§ N=14	0.4508 ± 0.0127 N=15	0.4026 * ± 0.0145 N=15

(continued)

Table 7-H. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Phenobarbital Treated F_1 Males (page 2 of 6)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Ventral Prostate Weight (g)[b]			
	0.2657 ‡ ± 0.0168 N=14	0.2772 ± 0.0220 N=15	0.2154 ± 0.0147 N=15
Dorsolateral Prostate Weight (g)[b]			
	0.1852 ± 0.0130 N=14	0.1585 ± 0.0134 N=15	0.1805 ± 0.0149 N=15
Prostate Weight (g)[b]			
	0.4509 ± 0.0258 N=14	0.4357 ± 0.0297 N=15	0.3959 ± 0.0267 N=15
Seminal Vesicles with Coagulating Glands Weight (g)[b]			
	0.6396 ‡ ± 0.0462 § N=13[d]	0.6410 ± 0.0428 N=15	0.4873 * ± 0.0344 N=15
Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[b]			
	0.6384 ‡‡ ± 0.0279 §§ N=14	0.6065 ± 0.0190 N=15	0.5252 ** ± 0.0237 N=15
Adjusted Pituitary Weight (g)[e]			
	0.0116 ± 0.0005 N=14	0.0105 ± 0.0005 N=14[c]	0.0105 ± 0.0006 N=13[c]
Adjusted Thyroid Weight (g)[e]			
	0.0268 ƱƱ ± 0.0013 ʎʎ N=14	0.0317 ƤƤ ± 0.0013 N=15	0.0332 ƤƤ ± 0.0013 N=15
Adjusted Liver Weight (g)[e]			
	16.6809 ƱƱƱ ± 0.3085 ʎʎʎ N=14	20.1385 ƤƤƤ ± 0.2907 N=15	22.9211 ƤƤƤ ± 0.3012 N=15

(continued)

Table 7-H. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Phenobarbital Treated F_1 Males (page 3 of 6)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Adjusted Paired Adrenal Gland Weight (g)[e]			
	0.0474 ± 0.0025 N=14	0.0528 ± 0.0023 N=15	0.0490 ± 0.0024 N=15
Adjusted Paired Kidney Weight (g)[e]			
	3.0108 ± 0.0553 N=14	3.0341 ± 0.0521 N=15	3.1031 ± 0.0540 N=15
Adjusted Paired Testis Weight (g)[e]			
	2.8482 ♂ ± 0.0470 ♂♂ N=14	2.7661 ± 0.0443 N=15	2.6658 ♀ ± 0.0459 N=15
Adjusted Paired Epididymis Weight (g)[e]			
	0.4507 ± 0.0142 ♂ N=14	0.4495 ± 0.0133 N=15	0.4091 ± 0.0138 N=15
Adjusted Ventral Prostate Weight (g)[e]			
	0.2572 ± 0.0184 N=14	0.2753 ± 0.0173 N=15	0.2252 ± 0.0179 N=15
Adjusted Dorsolateral Prostate Weight (g)[e]			
	0.1809 ± 0.0144 N=14	0.1576 ± 0.0136 N=15	0.1854 ± 0.0141 N=15
Adjusted Prostate Weight (g)[e]			
	0.4381 ± 0.0279 N=14	0.4329 ± 0.0263 N=15	0.4107 ± 0.0273 N=15
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[e]			
	0.6114 ± 0.0402 N=13[d]	0.6347 ± 0.0365 N=15	0.5180 ± 0.0378 N=15
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[e]			
	0.6226 ♂ ± 0.0226 ♂ N=14	0.6030 ± 0.0213 N=15	0.5434 ♀ ± 0.0221 N=15

(continued)

Table 7-H. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Phenobarbital Treated F_1 Males (page 4 of 6)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Adjusted Pituitary Weight (g)[f]			
	0.0117 ± 0.0005 N=14	0.0105 ± 0.0005 N=14[c]	0.0104 ± 0.0005 N=13[c]
Adjusted Thyroid Weight (g)[f]			
	0.0273 ♂ ± 0.0013 ♂♂ N=14	0.0319 ♀ ± 0.0013 N=15	0.0325 ♀ ± 0.0013 N=15
Adjusted Liver Weight (g)[f]			
	17.6425 ♂♂♂ ± 0.6799 ♂♂♂ N=14	20.3681 ♀ ± 0.6568 N=15	21.7942 ♀♀♀ ± 0.6572 N=15
Adjusted Paired Adrenal Gland Weight (g)[f]			
	0.0480 ± 0.0024 N=14	0.0530 ± 0.0023 N=15	0.0482 ± 0.0023 N=15
Adjusted Paired Kidney Weight (g)[f]			
	3.1177 ± 0.0852 N=14	3.0601 ± 0.0823 N=15	2.9773 ± 0.0823 N=15
Adjusted Paired Testis Weight (g)[f]			
	2.8702 ♂♂ ± 0.0434 ♂♂♂ N=14	2.7730 ± 0.0419 N=15	2.6383 ♀♀♀ ± 0.0419 N=15
Adjusted Paired Epididymis Weight (g)[f]			
	0.4570 ♂♂ ± 0.0133 ♂♂ N=14	0.4515 ± 0.0128 N=15	0.4012 ♀♀ ± 0.0128 N=15
Adjusted Ventral Prostate Weight (g)[f]			
	0.2666 ♂ ± 0.0174 ♂ N=14	0.2781 ± 0.0168 N=15	0.2136 ± 0.0168 N=15
Adjusted Dorsolateral Prostate Weight (g)[f]			
	0.1854 ± 0.0143 N=14	0.1587 ± 0.0138 N=15	0.1802 ± 0.0138 N=15

(continued)

Table 7-H. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Phenobarbital Treated F_1 Males (page 5 of 6)

	Phenobarbital (mg/kg/day, po)		
	0	50	100
Adjusted Prostate Weight (g)[f]			
	0.4520 ± 0.0273 N=14	0.4368 ± 0.0263 N=15	0.3938 ± 0.0264 N=15
Adjusted Seminal Vesicles with Coagulating Glands Weight (g)[f]			
	0.6400 ʊ ± 0.0434 ʎ N=13[d]	0.6416 ± 0.0404 N=15	0.4863 ʔ ± 0.0405 N=15
Adjusted Levator Ani plus Bulbcavernosus Muscle Complex Weight (g)[f]			
	0.6394 ʊʊ ± 0.0230 ʎʎʎ N=14	0.6076 ± 0.0222 N=15	0.5230 ʔʔ ± 0.0222 N=15
Thyroxine Hormone (T4) (ug/dL)[b]			
	5.78 ± 0.27 N=14	5.66 ± 0.26 N=15	5.73 ± 0.16 N=15
Thyroid Stimulating Hormone (TSH) (ng/ml)[b]			
	11.54 ± 0.90 N=14	16.37 ± 1.58 N=15	14.47 ± 1.61 N=15

(continued)

Table 7-H. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Phenobarbital Treated F_1 Males (page 6 of 6)

[a]Male 217 was found dead on postnatal day 31 prior to dosing (misdirected dose).
[b]Reported as the mean ± S.E.M.
[c]Decrease in N is due to one or more organ weights being statistical outliers and therefore they were excluded.
[d]Decrease in N is due to one seminal vesicles with coagulating glands inadvertently being nicked and leaking prior to weighing and therefore the weight was excluded.
[e]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[f]Reported as the adjusted mean ± S.E.M. (postnatal day 21 body weight as covariate).
‡p<0.05; ANOVA Test.
‡‡p<0.01; ANOVA Test.
‡‡‡p<0.001; ANOVA Test.
§p<0.05; Test for Linear Trend.
§§p<0.01; Test for Linear Trend.
§§§p<0.001; Test for Linear Trend.
*p<0.05; Dunnett's Test.
**p<0.01; Dunnett's Test.
***p<0.001; Dunnett's Test.
ʊp<0.05; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʊʊp<0.01; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʊʊʊp<0.001; Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎp<0.05; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎp<0.01; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
ʎʎʎp<0.001; Linear Trend Analysis of Covariance with body weight at sacrifice or on postnatal day 21 as the covariate.
⁎p<0.05; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
⁎⁎p<0.01; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.
⁎⁎⁎p<0.001; Dunnett's Test with body weight at sacrifice or on postnatal day 21 as the covariate.

Table 8-A. Summary of Necropsy Findings for the Atrazine-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	Atrazine (mg/kg/day, po)		
Finding	0	75	150
Epididymis: reduced in size, left		1	
Kidney: hydronephrosis, right	1	1	2
Testis: reduced in size, left		1	
undescended, left		1	

B. Unscheduled Necropsy

	Atrazine (mg/kg/day, po)		
Finding	0	75	150
Misdirected dose		1	

Table 8-B. Summary of Necropsy Findings for the p,p'-Dichlorodiphenyldichloroethylene-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	p,p'-Dichlorodiphenyldichloroethane (mg/kg/day, po)		
Finding	0	50	100
Chromodacryorrhea: nose			1
Intestines: distended with air			1
Kidney: hydronephrosis, bilateral			1
hydronephrosis, right	1	1	3

B. Unscheduled Necropsy

	p,p'-Dichlorodiphenyldichloroethane (mg/kg/day, po)		
Finding	0	50	100
Left metatarsal extremely swollen and edematous with ankle scabbed over and venous return appeared constricted by underlying tissue		1	

Table 8-C. Summary of Necropsy Findings for the Vinclozolin-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	Vinclozolin (mg/kg/day, po)		
Finding	0	30	100
Kidney: hydronephrosis, right	1	4	3
Seminal Vesicles: reduced in size			1

Table 8-D. Summary of Necropsy Findings for the Methoxychlor-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	Methoxychlor (mg/kg/day, po)		
Finding	0	25	50
Kidney: hydronephrosis, right	1		1

Table 8-E. Summary of Necropsy Findings for the Propylthiouracil-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	Propylthiouracil (mg/kg/day, po)		
Finding	0	2	25
Adrenal Gland: reduced in size, bilateral			4
Kidney: hydronephrosis, right		1	2
reduced in size, bilateral			1
Liver: mottled			2
reduced in size			4
Lungs: multiple foci		1	
Pituitary: reduced in size			1
Dorsolateral Prostate: reduced in size		1	1
Ventral Prostate: reduced in size		1	1
Seminal Vesicles: reduced in size, bilateral		1	
Thyroid: darkened and right side enlarged		1	
enlarged		3	2
enlarged, bilateral		1	4
enlarged and darkened		1	
enlarged and darkened, left side		1	
enlarged and reddened		1	3
enlarged and reddened, bilateral		1	5
Urinary Bladder: multiple 1 to 3 mm calculi and wall thickened	1		

B. Unscheduled Necropsy

	Propylthiouracil (mg/kg/day, po)		
Finding	0	2	25
Lungs: congested and oil present on cut surface, misdirected dose	1		
Trachea: oil present			1

Table 8-F. Summary of Necropsy Findings for the Ketoconazole-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	Ketoconazole (mg/kg/day, po)		
Finding	0	50	100
Adrenal Gland: dark tan/brown, bilateral		1	
enlarged, bilateral		1	5
enlarged, left			1
pale, bilateral		2	
Kidney: hydronephrosis, right		1	2
Lung: pinpoint foci, right			1
Dorsolateral Prostate: reduced in size		1	1
Ventral Prostate: reduced in size			3
Seminal Vesicle: reduced in size			1
Seminal Vesicles: reduced in size		1	1
reduced in size, bilateral			2
Urinary Bladder: multiple 1 to 3 mm calculi and wall thickened	1		

B. Unscheduled Necropsy

	Ketoconazole (mg/kg/day, po)		
Finding	0	50	100
Lungs: congested and oil present on cut surface, misdirected dose	1		
congested, dark red, small amount of corn oil on cut surface, misdirected dose			1

Table 8-G. Summary of Necropsy Findings for the Linuron-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	Linuron (mg/kg/day, po)		
Finding	0	50	100
Kidney: hydronephrosis, right			1
Lungs: multiple reddened areas			1
Pituitary: reduced in size			1
Dorsolateral Prostate: reduced in size		2	3
Ventral Prostate: reduced in size		2	4
Seminal Vesicle: reduced in size, right		1	
Seminal Vesicles: reduced in size			4
reduced in size, bilateral		2	2
Spleen: enlarged with white foci			1
Urinary Bladder: multiple 1 to 3 mm calculi and wall thickened	1		

B. Unscheduled Necropsy

	Linuron (mg/kg/day, po)		
Finding	0	50	100
Lungs: congested and oil present on cut surface, misdirected dose	1		

Table 8-H. Summary of Necropsy Findings for the Phenobarbital-Treated F_1 Males (page 1 of 1)

A. Scheduled Necropsy

	Phenobarbital (mg/kg/day, po)		
Finding	0	50	100
Kidney: hydronephrosis, right		2	2
Dorsolateral Prostate: reduced in size		1	2
Ventral Prostate: reduced in size		1	2
Seminal Vesicles: reduced in size			2
reduced in size, bilateral		1	1
Urinary Bladder: multiple 1 to 3 mm calculi and wall thickened	1		

B. Unscheduled Necropsy

	Phenobarbital (mg/kg/day, po)		
Finding	0	50	100
Lungs: congested and oil present on cut surface, misdirected dose	1		

APPENDIX 1

Individual Animal Data Tables

RTI INTERNATIONAL | **Memorandum**

Date: January 5, 2004

To: To the record

From: Julia D. George, Study Director

Subject: Correlation of treatment group designations within the documentation of RTI Study No. Rt02-ED03

During the course of this study, more than one set of designating numbers was used to denote the individual treatment groups in the two components. This memo serves to correlate the treatment group designations used in the different records of the report.

Study Protocol, RTI-831, Amendment 1

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)
		COMPONENT 1	
1	Corn oil (vehicle control)	0	0.0
2	Atrazine	75	15.0
3		150	30.0
4	p,p'DDE	50	10.0
5		100	20.0
6	Vinclozolin	30	6.0
7		100	20.0
8	Methoxychlor	25	5.0
9		50	10.0
		COMPONENT 2	
10	Propylthiouracil	2	0.4
11		25	5.0
12	Ketoconazole	50	10.0
13		100	20.0
14	Linuron	50	10.0
15		100	20.0
16	Phenobarbital	50	10.0
17		100	20.0
18	Finasteride[b]	25	5.0
19		50	10.0
20	Corn oil (vehicle control)	0	0.0

[a] Finasteride was unavailable, and was not tested in this study.

Dose Code Form/Study Data Sheets

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)	5 digit Rx Code	Color Code
			COMPONENT 1		
1	Corn oil (vehicle control)	0	0.0	78967	Orange
2	Methoxychlor	25	5.0	96509	Blue
3		50	10.0	68843	Red
4	Atrazine	75	15.0	84156	Purple
5		150	30.0	39239	Brown
6	4,4' DDE	50	10.0	29505	Pink
7		100	20.0	48266	Yellow
8	Vinclozolin	30	6.0	15492	Green
9		100	20.0	07983	Black
			COMPONENT 2		
1	Corn oil (vehicle control)	0	0.0	82703	Purple
2	Propylthiouracil	2	0.4	04691	Pink
3		25	5.0	65437	Black
4	Linuron	50	10.0	46916	Green
5		100	20.0	59969	Yellow
6	Ketoconazole	50	10.0	27489	Red
7		100	20.0	16317	Blue
8	Phenobarbital	50	10.0	34563	Orange
9		100	20.0	95962	Brown

Battelle, Sequim Formulation ID Number

Chemical	Concentration (mg/ml)	Formulation ID Number
	COMPONENT 1	
Corn oil (vehicle control)	0	2-14-H-M
Vinclozolin	6	2-14-J-M
	20	2-14-K-M
Methoxyclor	5	2-14-L-M
	10	2-14-M-M
4,4' DDE	10	2-14-N-M
	20	2-14-P-M
Atrazine	15	2-14-Q-M
	30	2-14-R-M
	COMPONENT 2	
Corn oil (vehicle control)	0	2-14-A-M
Propylthiouracil	0.4	2-14-B-M
	5	2-14-C-M
Linuron	10	2-14-D-M
	20	2-14-E-M
Ketoconazole	10	2-14-F-M
	20	2-14-G-M
Phenobarbital	10	2-14-H-M
	20	2-14-I-M

Histopathology report (EPL, Inc.)

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)
		COMPONENT 1	
1	Corn oil (vehicle control)	0	0.0
2	Methoxychlor	25	5.0
3		50	10.0
4	Atrazine	75	15.0
5		150	30.0
6	p,p'DDE	50	10.0
7		100	20.0
8	Vinclozolin	30	6.0
9		100	20.0
		COMPONENT 2	
1	Corn oil (vehicle control)	0	0.0
2	Propylthiouracil	2	0.4
3		25	5.0
4	Linuron	50	10.0
5		100	20.0
6	Ketoconazole	50	10.0
7		100	20.0
8	Phenobarbital	50	10.0
9		100	20.0

Appendix I – Individual Animal Data Tables

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)
		COMPONENT 1	
1	Corn oil (vehicle control)	0	0.0
2	Atrazine	75	15.0
3		150	30.0
4	p,p'DDE	50	10.0
5		100	20.0
6	Vinclozolin	30	6.0
7		100	20.0
8	Methoxychlor	25	5.0
9		50	10.0
10	Corn oil (vehicle control)	0	0.0
11	Propylthiouracil	2	0.4
12		25	5.0
13	Ketoconazole	50	10.0
14		100	20.0
15	Linuron	50	10.0
16		100	20.0
17	Phenobarbital	50	10.0
18		100	20.0

Table A-1. Individual F_1 Male Fate (page 1 of 7)

Group[a]	Animal ID	Phase of Study	Postnatal Day
1	1	Scheduled Sacrifice	52
	15	Scheduled Sacrifice	52
	32	Scheduled Sacrifice	52
	33	Scheduled Sacrifice	52
	50	Scheduled Sacrifice	52
	51	Scheduled Sacrifice	52
	68	Scheduled Sacrifice	52
	69[b]		
	86[b]		
	87	Scheduled Sacrifice	53
	104	Scheduled Sacrifice	53
	105	Scheduled Sacrifice	53
	122	Scheduled Sacrifice	53
	123	Scheduled Sacrifice	53
	135[b]		
2	4	Scheduled Sacrifice	52
	18[c]		
	29	Scheduled Sacrifice	52
	36	Scheduled Sacrifice	52
	47	Scheduled Sacrifice	52
	54	Post Wean Period	37
	65	Scheduled Sacrifice	52
	72	Scheduled Sacrifice	52
	83	Scheduled Sacrifice	53
	90	Scheduled Sacrifice	53
	101	Scheduled Sacrifice	53
	108	Scheduled Sacrifice	53
	119[b]		
	126	Scheduled Sacrifice	53
	133	Scheduled Sacrifice	53
3	5	Scheduled Sacrifice	52
	13	Scheduled Sacrifice	52
	19	Scheduled Sacrifice	52
	28	Scheduled Sacrifice	52
	37	Scheduled Sacrifice	52
	46	Scheduled Sacrifice	52
	55[b]		
	64	Scheduled Sacrifice	52
	73	Scheduled Sacrifice	52
	82	Scheduled Sacrifice	53
	91	Scheduled Sacrifice	53
	100	Scheduled Sacrifice	53
	109	Scheduled Sacrifice	53
	118[b]		
	127[b]		

(continued)

Table A-1. Individual F_1 Male Fate (page 2 of 7)

Group[a]	Animal ID	Phase of Study	Postnatal Day
4	6	Scheduled Sacrifice	52
	12	Scheduled Sacrifice	52
	20	Post Wean Period	29
	27	Scheduled Sacrifice	52
	38	Scheduled Sacrifice	52
	45	Scheduled Sacrifice	52
	56	Scheduled Sacrifice	52
	63	Scheduled Sacrifice	52
	74[b]		
	81	Scheduled Sacrifice	53
	92	Scheduled Sacrifice	53
	99	Scheduled Sacrifice	53
	110	Scheduled Sacrifice	53
	117	Scheduled Sacrifice	53
	128	Scheduled Sacrifice	53
5	7	Scheduled Sacrifice	52
	21	Scheduled Sacrifice	52
	26	Scheduled Sacrifice	52
	39	Scheduled Sacrifice	52
	44	Scheduled Sacrifice	52
	57	Scheduled Sacrifice	52
	62	Scheduled Sacrifice	52
	75	Scheduled Sacrifice	52
	80	Scheduled Sacrifice	53
	93	Scheduled Sacrifice	53
	98	Scheduled Sacrifice	53
	111	Scheduled Sacrifice	53
	116	Scheduled Sacrifice	53
	129	Scheduled Sacrifice	53
	132	Scheduled Sacrifice	53
6	8	Scheduled Sacrifice	52
	11	Scheduled Sacrifice	52
	22	Scheduled Sacrifice	52
	25	Scheduled Sacrifice	52
	40	Scheduled Sacrifice	52
	43	Scheduled Sacrifice	52
	58	Scheduled Sacrifice	52
	61	Scheduled Sacrifice	52
	76	Scheduled Sacrifice	53
	79[b]		
	94	Scheduled Sacrifice	53
	97	Scheduled Sacrifice	53
	112	Scheduled Sacrifice	53
	115[b]		
	130	Scheduled Sacrifice	53

(continued)

Table A-1. Individual F_1 Male Fate (page 3 of 7)

Group[a]	Animal ID	Phase of Study	Postnatal Day
7	9	Scheduled Sacrifice	52
	10	Scheduled Sacrifice	52
	23	Scheduled Sacrifice	52
	24[b]		
	41	Scheduled Sacrifice	52
	42	Scheduled Sacrifice	52
	59	Scheduled Sacrifice	52
	60	Scheduled Sacrifice	52
	77	Scheduled Sacrifice	53
	78	Scheduled Sacrifice	53
	95	Scheduled Sacrifice	53
	96	Scheduled Sacrifice	53
	113	Scheduled Sacrifice	53
	114[b]		
	131[b]		
8	2	Scheduled Sacrifice	52
	16	Scheduled Sacrifice	52
	31	Scheduled Sacrifice	52
	34	Scheduled Sacrifice	52
	49	Scheduled Sacrifice	52
	52	Scheduled Sacrifice	52
	67	Scheduled Sacrifice	52
	70	Scheduled Sacrifice	52
	85	Scheduled Sacrifice	53
	88	Scheduled Sacrifice	53
	103	Scheduled Sacrifice	53
	106	Scheduled Sacrifice	53
	121	Scheduled Sacrifice	53
	124	Scheduled Sacrifice	53
	134	Scheduled Sacrifice	53
9	3	Scheduled Sacrifice	52
	14	Scheduled Sacrifice	52
	17[b]		
	30[b]		
	35	Scheduled Sacrifice	52
	48	Scheduled Sacrifice	52
	53	Scheduled Sacrifice	52
	66	Scheduled Sacrifice	52
	71	Scheduled Sacrifice	52
	84	Scheduled Sacrifice	53
	89	Scheduled Sacrifice	53
	102	Scheduled Sacrifice	53
	107	Scheduled Sacrifice	53
	120	Scheduled Sacrifice	53
	125	Scheduled Sacrifice	53

(continued)

Table A-1. Individual F_1 Male Fate (page 4 of 7)

Group[a]	Animal ID	Phase of Study	Postnatal Day
10	136	Scheduled Sacrifice	52
	153	Scheduled Sacrifice	52
	154	Scheduled Sacrifice	52
	171	Scheduled Sacrifice	52
	172	Scheduled Sacrifice	52
	182	Scheduled Sacrifice	52
	199	Scheduled Sacrifice	52
	200	Scheduled Sacrifice	52
	217	Post Wean Period	31
	218	Scheduled Sacrifice	52
	235	Scheduled Sacrifice	53
	236	Scheduled Sacrifice	53
	253	Scheduled Sacrifice	53
	254	Scheduled Sacrifice	53
	270	Scheduled Sacrifice	53
11	137	Scheduled Sacrifice	52
	152	Scheduled Sacrifice	52
	155	Scheduled Sacrifice	52
	170	Scheduled Sacrifice	52
	173	Scheduled Sacrifice	52
	183	Scheduled Sacrifice	52
	198	Scheduled Sacrifice	52
	201	Scheduled Sacrifice	52
	216	Scheduled Sacrifice	52
	219	Scheduled Sacrifice	52
	234	Scheduled Sacrifice	53
	237	Scheduled Sacrifice	53
	252	Scheduled Sacrifice	53
	255	Scheduled Sacrifice	53
	269	Scheduled Sacrifice	53
12	138	Scheduled Sacrifice	52
	151	Scheduled Sacrifice	52
	156	Scheduled Sacrifice	52
	169	Scheduled Sacrifice	52
	174	Scheduled Sacrifice	52
	184	Scheduled Sacrifice	52
	197	Scheduled Sacrifice	52
	202	Scheduled Sacrifice	52
	215	Scheduled Sacrifice	52
	220	Scheduled Sacrifice	52
	233	Scheduled Sacrifice	53
	238	Scheduled Sacrifice	53
	251	Scheduled Sacrifice	53
	256	Scheduled Sacrifice	53
	268	Post Wean Period	50

(continued)

Table A-1. Individual F_1 Male Fate (page 5 of 7)

Group[a]	Animal ID	Phase of Study	Postnatal Day
13	141	Scheduled Sacrifice	52
	148	Scheduled Sacrifice	52
	159	Scheduled Sacrifice	52
	166	Scheduled Sacrifice	52
	177	Scheduled Sacrifice	52
	187	Scheduled Sacrifice	52
	194	Scheduled Sacrifice	52
	205	Scheduled Sacrifice	52
	212	Scheduled Sacrifice	52
	223	Scheduled Sacrifice	52
	230	Scheduled Sacrifice	53
	241	Scheduled Sacrifice	53
	248	Scheduled Sacrifice	53
	259	Scheduled Sacrifice	53
	265	Scheduled Sacrifice	53
14	142	Scheduled Sacrifice	52
	147	Scheduled Sacrifice	52
	160	Scheduled Sacrifice	52
	165	Scheduled Sacrifice	52
	178	Scheduled Sacrifice	52
	188	Scheduled Sacrifice	52
	193	Scheduled Sacrifice	52
	206	Scheduled Sacrifice	52
	211	Scheduled Sacrifice	52
	224	Scheduled Sacrifice	52
	229	Scheduled Sacrifice	53
	242	Post Wean Period	37
	247	Scheduled Sacrifice	53
	260	Scheduled Sacrifice	53
	264	Scheduled Sacrifice	53
15	139	Scheduled Sacrifice	52
	150	Scheduled Sacrifice	52
	157	Scheduled Sacrifice	52
	168	Scheduled Sacrifice	52
	175	Scheduled Sacrifice	52
	185	Scheduled Sacrifice	52
	196	Scheduled Sacrifice	52
	203	Scheduled Sacrifice	52
	214	Scheduled Sacrifice	52
	221	Scheduled Sacrifice	52
	232	Scheduled Sacrifice	53
	239	Scheduled Sacrifice	53
	250	Scheduled Sacrifice	53
	257	Scheduled Sacrifice	53
	267	Scheduled Sacrifice	53

(continued)

Table A-1. Individual F_1 Male Fate (page 6 of 7)

Group[a]	Animal ID	Phase of Study	Postnatal Day
16	140	Scheduled Sacrifice	52
	149	Scheduled Sacrifice	52
	158	Scheduled Sacrifice	52
	167	Scheduled Sacrifice	52
	176	Scheduled Sacrifice	52
	186	Scheduled Sacrifice	52
	195	Scheduled Sacrifice	52
	204	Scheduled Sacrifice	52
	213	Scheduled Sacrifice	52
	222	Scheduled Sacrifice	52
	231	Scheduled Sacrifice	53
	240	Scheduled Sacrifice	53
	249	Scheduled Sacrifice	53
	258	Scheduled Sacrifice	53
	266	Scheduled Sacrifice	53
17	143	Scheduled Sacrifice	52
	146	Scheduled Sacrifice	52
	161	Scheduled Sacrifice	52
	164	Scheduled Sacrifice	52
	179	Scheduled Sacrifice	52
	189	Scheduled Sacrifice	52
	192	Scheduled Sacrifice	52
	207	Scheduled Sacrifice	52
	210	Scheduled Sacrifice	52
	225	Scheduled Sacrifice	52
	228	Scheduled Sacrifice	53
	243	Scheduled Sacrifice	53
	246	Scheduled Sacrifice	53
	261	Scheduled Sacrifice	53
	263	Scheduled Sacrifice	53
18	144	Scheduled Sacrifice	52
	145	Scheduled Sacrifice	52
	162	Scheduled Sacrifice	52
	163	Scheduled Sacrifice	52
	180	Scheduled Sacrifice	52
	181	Scheduled Sacrifice	52
	190	Scheduled Sacrifice	52
	191	Scheduled Sacrifice	52
	208	Scheduled Sacrifice	52
	209	Scheduled Sacrifice	52
	226	Scheduled Sacrifice	52
	227	Scheduled Sacrifice	52
	244	Scheduled Sacrifice	53
	245	Scheduled Sacrifice	53
	262	Scheduled Sacrifice	53

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.
[b]Male was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Male was removed from the study because it was not dosed on the correct postnatal days.

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 1 of 10)

Group[a]	Animal ID	Postnatal Day										
		21	22	23	24	25	26	27	28	29	30	31
1	1	38.77	42.81	47.94	54.02	60.51	66.45	73.44	80.29	87.50	96.07	102.03
	15	53.35	57.55	65.10	71.02	76.68	79.84	84.54	91.31	98.13	105.00	111.60
	32	53.82	55.99	63.43	70.07	75.81	82.96	89.26	97.16	104.83	112.68	119.37
	33	55.27	58.80	67.00	74.16	79.83	84.59	91.02	100.55	105.52	114.15	120.06
	50	56.06	60.17	67.67	72.24	75.62	82.97	88.61	94.81	99.94	111.05	119.09
	51	56.79	58.39	62.87	67.50	74.18	79.54	86.46	92.50	99.47	106.10	114.67
	68	57.24	60.02	68.12	75.65	82.68	88.74	97.19	105.55	113.14	121.23	132.28
	69	.[b]										
	86	.[b]										
	87	58.71	64.54	72.11	79.63	89.73	95.17	103.98	111.26	122.12	131.78	142.08
	104	59.74	64.52	71.70	77.46	85.19	91.51	101.10	107.44	116.40	127.86	134.12
	105	59.85	63.90	69.58	76.77	84.59	91.39	98.25	104.50	112.95	121.75	130.79
	122	60.66	65.58	72.11	80.15	86.51	92.40	100.18	107.31	116.29	124.02	132.60
	123	61.35	64.32	71.00	77.92	83.23	89.70	94.42	103.28	106.81	117.14	124.00
	135	.[b]										
2	4	42.21	49.07	54.88	56.86	60.09	62.33	68.83	73.30	80.37	87.13	95.05
	18	.[c]										
	29	54.03	58.22	63.66	66.18	70.38	75.97	81.48	87.52	95.27	101.47	107.96
	36	55.25	60.19	65.94	68.73	75.66	82.20	88.80	95.88	103.04	110.21	118.06
	47	56.19	58.88	64.50	68.18	72.72	79.27	85.12	91.80	100.36	107.28	116.00
	54	56.40	59.46	64.85	67.26	73.56	79.60	83.53	89.76	97.25	104.15	111.97
	65	57.03	63.42	69.50	71.75	77.37	82.75	89.61	96.64	102.36	109.63	114.04
	72	57.26	62.74	66.99	68.38	74.49	80.86	88.41	96.84	105.10	113.33	122.00
	83	58.17	62.03	67.07	69.01	74.95	80.92	86.04	93.21	99.34	107.10	112.70
	90	58.76	64.58	70.20	73.89	79.05	87.33	93.67	101.98	106.45	117.53	104.69
	101	58.98	63.67	70.44	73.56	80.46	84.29	91.90	99.66	106.49	113.99	119.59
	108	59.89	63.74	69.33	71.18	75.73	80.11	86.65	92.60	99.25	107.23	114.00
	119	.[b]										
	126	60.82	65.75	70.65	73.41	79.02	83.81	91.00	95.78	102.80	110.18	118.52
	133	62.77	65.77	70.99	74.54	79.74	87.07	93.22	99.81	105.96	114.65	121.34

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 2 of 10)

Group[a]	Animal ID	Postnatal Day										
		21	22	23	24	25	26	27	28	29	30	31
3	5	41.91	45.32	50.85	52.88	55.21	62.16	61.84	67.12	73.13	78.28	85.34
	13	47.38	53.65	58.04	57.81	62.86	65.27	70.39	75.55	82.30	87.45	95.80
	19	54.94	60.48	64.52	63.77	65.45	68.86	75.83	82.20	90.92	96.03	104.02
	28	55.60	59.28	63.83	65.31	71.10	75.21	82.80	89.01	98.45	103.31	111.16
	37	55.93	61.78	65.83	66.89	67.32	73.51	80.88	87.95	95.30	102.12	109.22
	46	56.78	62.46	66.69	69.46	72.76	77.42	83.94	87.98	93.86	100.86	107.12
	55	.[b]										
	64	57.49	60.92	67.73	67.52	72.02	80.96	81.84	91.52	100.68	107.86	112.72
	73	58.42	63.42	69.21	68.82	70.85	76.92	84.90	90.01	97.73	104.12	110.14
	82	58.78	65.18	71.80	69.32	72.39	80.13	85.53	93.74	101.34	108.20	113.27
	91	59.14	66.15	71.80	72.21	73.89	79.02	86.03	92.77	100.47	108.48	115.27
	100	60.03	63.41	69.13	69.68	72.54	78.67	85.70	91.03	97.29	104.09	110.69
	109	60.75	65.44	73.21	72.55	76.18	81.81	84.00	92.34	103.15	108.53	112.08
	118	.[b]										
	127	.[b]										
4	6	38.89	43.36	47.96	53.10	57.83	63.10	68.96	72.97	77.97	84.24	91.95
	12	43.14	45.02	50.30	54.00	60.13	64.97	70.43	76.79	82.85	89.16	96.60
	20	54.02	57.58	59.63	65.32	71.40	65.31	76.87	83.76	90.89	.[d]	
	27	55.80	59.87	66.11	72.01	80.43	87.79	94.45	102.98	110.88	117.57	125.90
	38	56.26	60.49	65.99	72.42	78.99	85.46	92.40	102.04	109.50	117.55	123.81
	45	56.42	59.75	63.86	70.30	75.21	82.10	88.15	93.12	103.55	110.16	117.09
	56	57.15	63.60	68.76	75.26	81.84	87.33	95.14	101.90	111.03	118.83	126.33
	63	57.89	63.06	67.78	73.66	81.23	88.37	95.46	103.43	111.56	119.31	128.86
	74	.[b]										
	81	58.64	60.99	67.84	75.39	81.84	87.25	94.04	101.30	108.30	114.30	122.42
	92	59.24	65.76	70.62	75.36	81.36	88.44	94.78	101.99	109.00	116.27	124.32
	99	59.96	65.66	73.20	76.66	84.30	91.33	98.00	106.61	113.65	124.25	134.60
	110	60.51	64.41	70.27	76.02	82.63	90.21	96.56	103.42	110.11	119.37	126.42
	117	61.34	64.68	70.61	77.00	83.76	90.80	98.17	105.49	112.98	122.79	113.92
	128	63.44	67.32	72.00	77.89	86.18	92.62	102.19	110.66	118.07	127.94	137.00

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 3 of 10)

Group[a]	Animal ID	Postnatal Day										
		21	22	23	24	25	26	27	28	29	30	31
5	7	36.87	39.27	44.54	48.42	52.70	59.07	63.72	70.15	75.10	84.90	91.20
	21	53.16	58.42	64.74	72.40	78.74	87.35	93.50	103.00	112.67	123.92	129.64
	26	54.89	56.62	60.24	65.64	73.09	80.87	85.60	93.35	104.14	113.25	119.33
	39	55.25	58.81	63.05	69.54	76.41	82.31	88.80	97.62	104.14	114.26	119.92
	44	55.94	59.14	63.82	70.34	74.58	80.72	88.24	94.92	102.14	111.20	116.38
	57	56.69	61.56	64.93	71.57	77.07	84.87	91.02	98.62	106.72	114.10	122.42
	62	57.07	61.11	66.04	68.41	73.18	78.10	85.73	92.07	101.10	106.46	112.86
	75	57.97	63.40	68.57	73.04	78.40	86.14	90.70	98.42	108.00	115.10	121.18
	80	58.32	52.44	56.72	62.22	68.20	74.90	80.22	87.07	94.66	102.28	110.28
	93	58.73	61.42	66.96	70.34	78.18	84.39	88.11	96.66	106.74	113.84	120.89
	98	59.47	63.62	69.08	73.70	82.50	88.88	94.62	103.77	111.95	118.81	127.40
	111	59.88	62.56	68.46	70.57	78.42	86.17	94.40	100.32	110.50	119.47	127.96
	116	60.61	66.88	73.78	79.74	87.08	95.60	100.45	110.32	119.80	128.12	138.72
	129	61.55	66.85	73.65	79.51	87.76	95.43	104.45	112.25	121.12	130.56	138.12
	132	61.98	66.05	70.66	77.37	82.82	91.85	97.70	108.45	115.32	122.60	133.04
6	8	41.39	46.38	52.50	57.44	61.22	65.49	72.03	78.71	84.65	91.83	99.68
	11	45.16	47.58	53.71	59.58	65.29	70.41	76.35	82.18	88.73	95.25	102.69
	22	54.30	59.94	64.45	69.45	78.74	86.06	93.86	102.24	109.22	119.88	126.98
	25	55.49	60.51	65.10	71.28	77.47	84.04	88.99	94.75	101.67	107.45	115.45
	40	55.96	61.02	67.50	74.28	80.12	87.89	94.20	101.97	109.21	117.44	124.37
	43	56.56	59.90	65.15	71.78	77.04	83.25	88.84	95.11	101.03	110.63	116.75
	58	56.79	58.00	61.05	66.40	72.79	80.33	87.45	93.10	99.90	108.16	117.31
	61	57.74	62.60	69.22	76.25	83.46	88.41	98.66	105.96	114.12	123.88	133.26
	76	58.23	62.23	68.58	75.03	79.45	85.92	91.18	98.54	105.38	113.10	120.98
	79	.[b]										
	94	58.85	69.24	73.70	79.87	87.24	93.61	100.30	107.23	116.26	123.66	134.19
	97	60.07	63.57	71.43	76.67	81.77	88.84	94.20	101.49	108.74	117.50	124.46
	112	60.35	66.25	70.89	76.28	84.02	89.95	97.43	105.31	113.77	121.09	130.17
	115	.[b]										
	130	61.68	68.39	74.83	81.51	89.36	96.93	104.33	113.71	123.19	131.91	139.49

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 4 of 10)

Group[a]	Animal ID	Postnatal Day										
		21	22	23	24	25	26	27	28	29	30	31
7	9	38.28	42.14	49.03	53.52	59.41	64.61	71.07	78.12	84.92	90.54	97.85
	10	47.97	50.63	58.01	62.31	66.04	74.50	79.70	86.66	92.50	100.71	107.13
	23	54.38	58.21	63.66	68.42	74.56	81.19	87.68	95.40	103.02	112.63	105.84
	24	.[b]										
	41	55.98	60.40	65.89	71.09	75.99	82.33	89.44	96.87	104.57	111.09	106.04
	42	56.29	61.91	66.30	72.07	79.32	86.29	92.78	98.80	105.70	112.56	121.27
	59	56.92	59.23	64.70	68.55	74.80	80.44	87.56	94.13	102.06	109.38	117.03
	60	57.57	59.67	65.67	68.42	76.08	81.48	86.45	94.27	103.57	110.11	116.94
	77	58.28	61.45	67.36	73.06	80.34	82.50	87.53	96.18	103.75	108.92	113.59
	78	58.72	64.95	70.94	74.88	82.59	89.78	96.50	103.63	112.97	120.73	128.81
	95	58.88	63.57	68.53	73.27	79.81	85.61	91.76	100.74	106.81	114.75	124.61
	96	60.31	65.22	70.79	74.39	81.93	88.49	95.12	102.69	112.24	121.10	129.98
	113	60.49	66.62	71.64	76.19	82.56	89.83	97.61	103.94	111.89	117.64	126.85
	114	.[b]										
	131	.[b]										
8	2	39.30	42.12	47.20	53.10	58.46	64.50	70.35	76.60	82.40	88.45	95.40
	16	53.61	56.52	64.87	71.14	77.30	84.08	92.55	98.62	108.58	119.10	129.42
	31	54.53	58.36	64.03	69.18	77.12	83.41	93.58	98.57	107.65	116.21	108.80
	34	55.17	59.12	66.17	71.30	78.18	84.82	91.05	99.50	106.73	116.36	123.83
	49	55.87	55.30	62.71	70.25	76.90	83.65	90.68	98.33	107.49	117.11	124.90
	52	56.29	57.72	63.81	72.25	79.66	87.02	96.02	105.82	114.54	124.52	132.83
	67	57.17	60.80	67.29	73.19	78.73	84.74	91.05	99.33	103.11	111.76	117.62
	70	57.43	60.90	69.14	74.42	82.21	88.51	98.80	104.93	114.81	123.59	129.72
	85	58.43	63.00	70.20	74.32	81.89	88.26	96.34	102.20	109.83	119.26	125.88
	88	58.82	63.60	71.08	76.85	83.59	89.94	97.28	104.77	112.18	121.55	129.84
	103	59.84	65.54	72.14	78.63	83.81	91.54	98.68	105.35	111.82	119.56	125.90
	106	59.99	63.02	70.35	75.81	84.59	90.53	97.61	104.32	111.93	119.10	129.14
	121	60.63	64.35	70.50	75.61	82.91	89.57	96.13	105.25	112.05	120.66	127.50
	124	61.29	62.49	70.18	78.06	83.48	90.25	98.92	106.35	112.94	119.19	129.22
	134	63.07	65.52	72.66	78.99	84.17	92.14	99.59	107.07	114.25	123.35	130.41

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 5 of 10)

Group[a]	Animal ID	Postnatal Day										
		21	22	23	24	25	26	27	28	29	30	31
9	3	37.88	41.44	47.57	51.21	58.76	64.03	70.51	75.95	81.06	88.23	94.26
	14	44.30	46.14	50.66	54.64	60.25	66.77	72.90	78.25	84.15	89.25	98.59
	17	.[b]										
	30	.[b]										
	35	55.99	61.83	67.92	73.37	78.45	84.00	91.50	99.42	105.71	112.98	120.26
	48	56.34	61.12	64.56	71.99	78.75	84.53	92.03	100.45	105.77	114.09	121.66
	53	56.85	57.41	61.14	68.53	76.33	82.61	89.29	98.16	103.05	109.75	119.77
	66	57.86	61.77	67.00	71.83	81.00	86.64	92.37	100.47	108.71	118.42	125.10
	71	58.12	63.71	69.62	75.74	82.47	89.23	97.99	106.21	115.58	122.06	126.00
	84	58.54	63.82	69.60	75.93	83.64	90.40	97.85	104.19	114.62	123.50	130.60
	89	59.71	63.69	69.75	75.66	82.85	90.78	98.98	107.04	115.78	120.30	128.02
	102	59.89	63.62	70.70	78.54	85.94	93.21	101.38	110.85	118.53	129.50	136.72
	107	60.77	67.17	74.00	80.65	88.62	97.60	103.87	109.25	118.67	129.45	135.70
	120	61.61	66.22	74.17	79.52	87.42	94.70	104.23	109.30	120.21	129.50	138.08
	125	62.65	66.52	73.47	80.23	84.42	92.35	101.09	108.73	116.20	124.87	131.85
10	136	44.55	45.95	51.97	57.42	62.65	67.67	74.21	79.63	87.25	93.50	99.25
	153	49.80	52.72	60.61	66.51	72.03	77.75	84.08	91.01	97.63	104.03	113.57
	154	50.58	55.02	61.62	68.36	74.79	83.14	87.57	96.70	104.21	113.00	121.03
	171	56.10	58.73	66.22	72.59	76.30	81.84	89.12	95.24	103.80	110.91	118.78
	172	62.74	65.15	71.15	76.26	83.84	88.59	96.10	103.26	110.84	118.30	125.94
	182	55.86	61.32	68.60	74.86	81.42	88.80	97.60	106.78	116.58	126.52	133.44
	199	56.75	62.71	69.98	75.54	81.97	88.34	93.39	96.01	105.48	116.31	122.56
	200	57.39	62.01	67.83	75.23	82.79	90.35	98.06	108.12	116.30	123.75	127.59
	217	57.92	62.96	69.32	74.60	79.82	87.03	94.59	103.08	109.48	115.88	.[e]
	218	58.56	61.34	68.71	74.80	81.32	87.52	95.26	101.90	110.32	117.66	124.52
	235	59.69	65.19	71.46	77.27	85.94	93.48	101.97	109.85	118.05	126.48	134.90
	236	59.84	63.42	70.25	74.89	83.34	89.20	96.32	106.25	112.62	120.47	131.58
	253	60.79	61.52	67.20	73.77	80.90	85.78	93.15	101.87	108.49	114.24	122.29
	254	61.78	63.30	71.91	79.15	87.33	94.47	101.35	109.29	117.32	125.85	136.57
	270	62.43	66.23	72.60	79.08	87.81	93.72	102.33	110.67	119.31	128.69	137.76

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 6 of 10)

		Postnatal Day										
Group[a]	Animal ID	21	22	23	24	25	26	27	28	29	30	31
11	137	46.70	47.76	55.19	60.78	67.97	77.21	83.68	91.44	98.49	104.62	111.63
	152	50.39	53.12	59.67	66.29	73.87	79.86	85.75	95.39	104.27	109.31	119.42
	155	51.09	54.55	61.12	68.13	75.40	83.94	92.19	101.20	109.43	117.45	126.62
	170	52.95	58.22	64.55	72.29	79.75	85.79	93.72	98.94	107.54	117.04	124.48
	173	58.84	63.51	70.92	78.04	86.43	92.46	100.54	109.89	118.23	128.13	136.03
	183	55.08	57.81	63.32	70.28	76.93	82.31	88.40	95.54	101.58	106.79	117.50
	198	56.72	59.44	66.66	73.75	81.10	87.84	95.30	103.22	113.45	121.47	128.49
	201	56.89	60.88	67.69	74.82	82.32	87.69	96.33	104.38	111.12	117.68	128.94
	216	58.17	64.46	69.58	75.67	82.90	90.50	96.79	106.93	113.14	120.59	128.32
	219	58.78	60.42	66.63	73.98	80.89	87.63	95.87	105.47	111.68	118.29	127.91
	234	59.80	66.79	71.01	78.06	85.46	92.52	98.88	106.72	113.74	120.22	128.91
	237	60.11	61.37	68.28	75.56	83.02	89.38	96.83	105.10	113.45	122.43	129.52
	252	60.70	66.67	75.46	81.70	89.72	97.91	105.70	113.48	122.33	132.18	138.63
	255	61.50	65.24	73.51	79.68	88.33	94.68	100.75	109.44	116.25	124.63	134.18
	269	63.05	69.25	73.88	80.94	88.69	95.52	102.74	110.40	117.38	127.96	137.51
12	138	43.70	47.56	53.00	59.45	65.88	69.33	77.55	84.59	89.95	94.39	98.54
	151	48.12	52.32	58.47	67.45	72.88	79.92	84.13	91.00	96.69	99.99	104.84
	156	51.34	52.41	57.95	65.02	71.60	78.23	85.68	92.55	99.64	103.25	111.68
	169	56.31	60.25	65.04	71.32	77.21	86.56	90.85	93.66	108.02	114.30	121.94
	174	62.30	65.26	72.54	78.58	87.79	94.13	100.26	110.20	117.89	127.09	133.78
	184	55.23	60.22	65.47	71.93	79.03	87.45	94.15	101.42	108.20	114.67	120.95
	197	56.02	59.99	64.23	70.08	75.17	82.31	87.90	96.07	102.58	109.48	115.03
	202	57.39	62.97	68.45	74.49	81.33	88.55	94.90	103.15	109.10	112.55	123.52
	215	57.64	62.17	69.06	75.48	83.58	89.41	99.94	108.02	114.35	121.19	132.01
	220	58.32	61.76	68.08	74.35	81.37	88.35	91.28	105.08	110.46	119.99	129.14
	233	59.60	64.06	70.81	77.50	85.33	92.25	99.35	110.56	115.12	123.36	131.56
	238	59.88	63.95	70.15	75.67	82.77	91.84	99.40	111.22	119.48	124.58	133.71
	251	61.14	62.24	66.39	73.10	80.51	85.79	92.83	100.16	106.80	113.82	121.59
	256	62.05	65.71	73.46	79.38	84.27	90.25	96.38	106.71	114.29	122.22	129.29
	268	62.80	68.10	73.38	78.62	87.26	93.18	102.16	108.62	113.68	121.22	127.45

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 7 of 10)

Group[a]	Animal ID	Postnatal Day										
		21	22	23	24	25	26	27	28	29	30	31
13	141	46.10	49.87	51.90	58.07	65.15	72.07	78.73	85.21	92.61	99.77	106.55
	148	48.04	51.09	56.93	63.64	70.11	76.63	84.71	93.82	101.95	111.31	120.52
	159	50.62	54.59	59.39	66.11	72.19	76.80	82.27	88.62	96.58	103.60	109.55
	166	57.43	62.02	66.60	71.46	78.76	84.69	91.67	99.13	107.44	115.45	124.54
	177	63.34	65.66	70.36	77.98	86.45	93.23	100.33	108.63	117.53	126.86	136.35
	187	55.36	57.90	67.47	73.61	80.29	86.80	93.41	100.30	107.27	115.27	124.09
	194	56.61	54.15	60.24	65.11	71.13	78.69	84.68	90.83	97.52	104.32	112.39
	205	57.40	62.13	69.69	77.15	81.11	88.60	94.50	100.49	108.15	115.77	125.63
	212	58.29	63.53	68.85	77.67	82.52	87.06	96.88	103.41	114.02	124.97	131.11
	223	58.56	62.37	70.31	75.66	83.05	89.59	97.26	105.63	112.02	120.42	129.93
	230	59.43	62.55	67.88	73.44	79.10	84.77	90.73	98.15	103.70	111.54	119.22
	241	59.88	61.96	71.69	78.88	85.98	92.64	100.87	109.66	119.12	128.49	137.11
	248	60.65	61.32	68.32	73.90	82.61	86.71	94.74	102.75	110.97	117.41	126.69
	259	61.53	64.47	71.66	78.22	85.91	94.54	100.96	109.19	117.44	127.65	137.87
	265	63.15	62.33	74.50	80.58	89.69	94.51	103.87	113.36	122.14	128.76	137.03
14	142	43.18	46.90	50.80	56.38	63.55	69.79	76.10	82.19	90.09	95.80	103.38
	147	49.25	53.54	59.64	64.73	71.03	75.63	82.44	89.44	97.52	103.76	111.86
	160	52.25	55.81	61.17	65.19	71.65	78.85	82.70	90.89	97.47	103.63	111.37
	165	53.50	56.33	59.33	65.24	72.38	76.50	82.71	87.89	93.45	99.81	104.75
	178	59.49	61.47	70.86	74.61	82.00	89.80	96.51	103.30	109.35	118.32	127.84
	188	55.74	59.16	65.83	70.13	74.94	81.31	86.14	93.45	100.97	108.65	117.41
	193	56.18	57.38	66.52	72.13	78.42	85.01	91.09	96.96	106.16	113.61	120.45
	206	57.61	60.60	69.38	75.24	79.18	86.10	90.17	100.00	108.60	114.65	125.07
	211	58.13	60.54	68.41	72.02	78.26	84.24	91.35	99.41	105.17	113.71	122.51
	224	58.65	61.92	68.81	74.19	79.04	84.27	89.25	98.04	103.81	112.55	120.36
	229	59.60	61.46	68.54	74.01	80.88	87.11	95.16	103.12	110.87	119.32	128.48
	242	59.84	63.48	71.12	77.49	82.74	88.55	96.13	103.49	111.37	119.19	126.66
	247	60.68	65.76	73.83	78.69	84.60	90.71	99.16	107.40	114.15	123.51	131.90
	260	61.91	61.06	66.91	73.51	80.53	88.06	96.55	103.48	114.90	119.82	131.87
	264	62.46	65.48	74.74	80.02	86.07	93.98	103.33	110.39	117.48	126.77	136.32

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 8 of 10)

		Postnatal Day										
Group[a]	Animal ID	21	22	23	24	25	26	27	28	29	30	31
15	139	47.66	50.76	57.00	62.27	67.55	72.85	79.22	88.03	92.71	99.12	105.28
	150	50.10	52.88	59.65	64.89	69.88	75.45	80.81	85.55	94.40	101.81	108.47
	157	50.63	54.12	59.70	64.06	70.17	73.96	79.89	85.46	91.98	97.64	104.34
	168	55.14	57.62	66.48	70.40	76.10	81.47	88.31	95.49	103.98	112.62	118.94
	175	62.77	66.28	72.16	77.52	81.17	87.09	92.08	98.42	106.06	111.63	118.40
	185	55.34	57.61	65.29	68.78	75.56	81.92	87.19	95.50	102.25	109.27	119.24
	196	56.09	61.70	69.75	74.54	78.94	87.48	89.81	101.90	109.17	117.22	125.30
	203	56.81	58.43	65.37	69.07	74.98	80.63	88.51	94.30	102.64	109.19	117.93
	214	57.65	60.36	66.55	70.96	75.69	77.49	82.58	91.17	97.99	101.31	110.16
	221	58.73	64.56	71.91	73.19	78.41	85.04	91.51	100.35	104.98	114.45	119.98
	232	59.07	60.20	67.76	73.06	77.85	82.34	85.41	97.57	103.22	112.20	117.12
	239	59.86	62.47	72.66	73.40	81.53	88.28	94.55	104.14	112.43	120.11	125.27
	250	61.00	63.74	70.45	74.60	80.72	87.30	93.42	98.66	104.81	112.72	120.97
	257	61.28	66.21	73.88	78.07	86.49	91.45	100.52	109.50	116.50	123.31	132.31
	267	62.80	62.52	68.09	74.74	80.22	84.76	91.12	100.33	107.71	115.00	124.86
16	140	47.43	51.61	57.84	62.20	67.28	72.84	79.18	85.12	88.61	97.48	103.74
	149	48.90	51.74	57.06	59.13	64.50	68.48	74.91	79.73	84.18	92.57	98.71
	158	52.59	56.52	62.86	67.41	72.69	76.78	82.49	88.30	96.29	103.32	109.61
	167	57.35	59.58	62.00	61.53	62.63	68.23	72.36	77.65	83.49	89.89	94.89
	176	59.29	63.17	67.30	73.29	79.13	83.68	89.77	97.26	105.59	112.45	117.27
	186	55.75	58.25	64.55	68.92	74.74	79.87	86.35	94.28	100.24	107.75	114.30
	195	56.06	53.80	65.94	69.59	75.19	82.53	89.04	96.95	104.64	110.54	115.77
	204	57.01	58.06	62.44	65.83	72.09	76.60	81.70	87.84	93.75	99.85	106.03
	213	58.16	61.10	67.74	69.08	73.46	77.84	82.68	89.85	95.22	99.75	106.70
	222	58.76	59.86	65.11	69.43	73.94	80.12	85.20	93.46	100.69	107.18	114.46
	231	59.23	59.15	66.21	67.55	71.59	77.23	82.13	88.97	92.05	96.05	103.26
	240	60.32	60.12	65.70	70.04	76.92	81.45	87.72	95.50	103.70	110.74	119.40
	249	60.92	66.20	74.05	75.02	80.76	85.72	91.45	98.84	103.37	109.46	116.07
	258	61.72	69.25	72.18	77.55	84.97	88.64	97.51	106.55	114.01	121.38	129.24
	266	62.70	64.89	73.08	79.32	84.04	89.18	94.35	102.08	110.67	118.90	125.91

(continued)

Table A-2. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 21 Through 31 (page 9 of 10)

		Postnatal Day										
Group[a]	Animal ID	21	22	23	24	25	26	27	28	29	30	31
17	143	47.12	50.17	55.12	61.52	67.73	72.34	78.36	84.92	91.70	99.81	107.66
	146	48.48	50.97	54.84	63.85	70.81	76.10	83.33	90.26	98.01	105.47	113.43
	161	50.71	55.19	62.37	69.09	75.71	80.22	87.73	96.14	101.92	109.89	116.91
	164	57.07	62.39	67.09	73.86	82.36	88.44	96.42	104.66	111.90	123.25	132.79
	179	61.73	66.29	73.99	82.28	88.19	96.31	105.93	112.41	120.05	129.08	139.66
	189	55.36	56.54	65.82	73.29	78.50	84.31	90.88	96.57	103.89	112.35	119.32
	192	55.90	56.85	65.09	75.43	84.18	90.67	97.63	104.95	117.55	126.50	135.36
	207	57.32	60.78	68.25	76.84	81.34	87.12	95.28	101.42	108.97	117.06	125.15
	210	57.66	59.55	68.13	72.42	76.39	81.51	87.06	93.00	99.44	106.26	112.23
	225	58.68	64.82	73.42	79.61	84.87	91.82	99.91	106.54	115.50	123.11	131.50
	228	58.84	60.52	69.37	76.36	81.13	87.45	94.00	98.71	109.36	116.46	123.07
	243	60.39	65.13	72.40	79.80	86.36	92.26	100.04	108.58	117.57	126.28	135.23
	246	60.57	62.54	71.56	78.68	84.00	89.84	94.79	102.03	109.80	114.55	122.25
	261	61.49	57.57	68.20	76.02	82.50	88.95	92.12	101.74	109.87	116.49	123.63
	263	62.26	64.87	72.38	79.95	85.34	92.37	99.27	106.06	114.18	123.21	131.39
18	144	44.23	47.72	53.01	59.19	63.55	69.85	75.66	83.91	90.41	97.40	104.54
	145	49.04	52.61	57.28	64.33	70.51	75.50	82.26	87.93	93.92	104.70	111.10
	162	50.79	53.19	57.84	64.74	71.67	76.32	82.94	88.68	93.94	101.53	107.57
	163	56.79	61.40	64.78	70.87	76.12	80.13	86.40	93.54	100.52	110.62	118.27
	180	61.92	64.32	69.83	76.37	82.37	86.14	94.07	99.61	106.35	114.67	121.32
	181	64.22	64.63	66.92	74.56	80.12	85.03	88.72	93.19	98.76	105.20	110.90
	190	56.09	57.19	66.98	73.29	79.29	84.98	90.40	96.68	105.32	112.11	119.13
	191	57.07	56.14	64.88	72.12	75.85	82.14	88.62	94.44	102.20	108.78	116.04
	208	57.86	60.90	68.33	75.82	80.52	85.48	95.38	101.92	109.15	118.35	124.33
	209	58.57	62.66	71.52	77.34	82.51	87.62	95.30	102.52	112.69	119.36	125.81
	226	59.00	63.27	72.91	80.88	86.98	91.95	99.85	109.29	118.01	128.01	135.59
	227	60.56	64.36	72.48	78.21	84.21	87.55	95.72	102.11	111.87	119.26	126.87
	244	60.61	64.92	72.69	79.39	83.15	89.80	97.53	104.89	113.97	123.44	130.12
	245	62.11	64.52	72.61	79.02	84.03	89.76	96.02	102.18	110.84	118.21	124.44
	262	62.72	63.61	70.30	80.32	85.77	92.33	99.41	100.49	109.15	104.13	108.61

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.

[b]Male was removed from the study because his correct postnatal day 0 could not be confirmed.

[c]Male was removed from the study because it was not dosed on the correct postnatal days.

[d]Male was euthanized on postnatal day 29 after dosing due to a leg injury.

[e]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 1 of 10)

Group[a]	Animal ID	Postnatal Day										
		32	33	34	35	36	37	38	39	40	41	42
1	1	109.82	120.49	127.89	137.29	146.15	157.05	167.57	177.72	186.02	193.45	200.26
	15	120.92	127.99	135.96	147.91	155.94	161.08	173.63	181.08	190.40	197.94	206.13
	32	130.62	138.61	148.72	157.41	171.00	180.44	189.11	197.29	207.57	206.83	215.55
	33	128.82	139.14	145.86	155.03	165.86	176.38	185.00	188.37	199.01	205.43	219.86
	50	130.59	140.56	150.52	158.51	170.10	180.77	192.22	202.55	211.21	219.97	229.20
	51	122.40	130.21	141.27	152.16	161.46	170.55	179.33	187.42	198.35	206.65	213.25
	68	140.54	146.82	155.60	167.45	178.72	185.51	195.10	204.28	212.40	218.80	231.20
	69	.[b]										
	86	.[b]										
	87	152.83	163.96	173.82	182.45	197.00	204.04	217.30	226.06	233.18	239.20	253.00
	104	144.66	155.76	164.24	176.66	189.35	200.57	212.46	217.50	228.57	236.78	253.47
	105	140.77	149.16	162.84	169.86	180.75	189.60	200.22	209.51	218.73	233.56	246.13
	122	138.29	148.91	158.12	166.85	174.71	185.44	194.13	198.72	209.90	221.71	224.12
	123	132.61	141.31	149.80	157.69	166.49	174.43	186.04	193.41	200.95	211.76	216.45
	135	.[b]										
2	4	101.88	109.70	115.55	123.19	134.72	143.90	149.25	160.35	164.09	173.66	182.36
	18	.[c]										
	29	117.64	127.00	134.27	146.78	156.32	166.09	171.81	179.80	186.26	195.66	202.17
	36	126.73	134.44	143.06	153.19	161.54	170.11	179.10	185.12	194.10	200.52	210.46
	47	126.62	134.50	143.27	154.61	163.10	171.80	178.98	185.09	194.04	200.10	209.10
	54	120.62	130.44	137.23	146.96	157.23	166.59	.[d]				
	65	123.77	132.46	140.26	150.15	159.84	167.15	175.60	186.14	192.09	201.90	207.47
	72	131.02	140.47	150.83	159.52	169.44	175.53	188.12	195.91	204.31	211.30	219.27
	83	122.24	130.82	139.15	148.72	159.50	167.00	172.50	182.47	188.75	194.88	203.84
	90	120.00	96.16	127.05	136.18	149.00	163.49	168.43	179.15	187.78	197.45	203.16
	101	127.64	137.17	144.58	152.91	168.42	173.78	182.97	192.41	199.54	206.00	219.15
	108	.[e]	130.64	140.39	150.12	161.00	174.04	180.20	189.00	194.29	205.60	213.09
	119	.[b]										
	126	128.00	132.43	141.72	149.99	165.03	170.00	177.50	188.24	190.85	200.35	209.25
	133	130.66	142.18	148.06	158.12	169.80	175.14	186.31	193.00	202.47	210.44	217.17

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 2 of 10)

Group[a]	Animal ID	Postnatal Day										
		32	33	34	35	36	37	38	39	40	41	42
3	5	91.50	97.11	106.10	112.27	121.53	130.76	136.46	143.30	151.04	156.56	171.66
	13	99.15	106.00	115.17	123.75	132.05	142.23	146.19	150.56	168.24	173.16	182.02
	19	113.15	120.32	132.10	138.27	152.49	156.03	162.45	175.50	185.50	194.75	197.41
	28	120.40	127.99	137.82	147.12	156.45	164.79	166.65	179.22	184.99	211.60	194.88
	37	116.49	123.75	129.20	139.28	151.44	157.28	165.70	171.23	180.25	186.20	192.15
	46	109.90	121.97	129.11	139.16	148.17	155.15	163.83	170.45	175.86	184.32	190.86
	55	.[b]										
	64	119.50	124.99	132.01	142.13	153.95	157.95	165.62	176.29	184.65	193.50	199.87
	73	120.92	130.44	137.48	151.37	162.24	167.02	172.56	180.54	190.10	193.13	200.66
	82	121.80	127.69	137.18	144.68	154.86	163.30	173.41	180.25	186.81	194.84	204.39
	91	123.47	132.16	141.02	150.06	164.48	166.20	172.48	183.74	193.93	204.35	207.14
	100	118.99	125.34	134.06	145.43	152.54	161.91	169.22	176.15	186.30	190.26	196.17
	109	120.97	126.78	133.98	145.43	154.69	159.15	165.40	173.62	179.26	183.81	191.88
	118	.[b]										
	127	.[b]										
4	6	95.11	103.21	110.98	119.86	127.67	137.35	144.60	151.50	163.10	167.44	179.60
	12	101.52	110.94	119.87	126.36	136.20	145.72	155.40	162.99	173.81	182.60	188.82
	20	.[f]										
	27	136.16	144.71	155.02	163.19	171.94	182.66	191.70	201.30	209.91	218.32	227.44
	38	135.07	144.80	155.17	164.63	171.60	183.51	193.94	202.10	213.91	224.28	232.58
	45	126.60	134.27	145.53	153.84	162.61	171.49	181.19	190.64	203.40	212.65	219.44
	56	137.62	147.49	158.78	166.57	179.92	190.80	196.12	205.66	219.95	227.07	235.12
	63	136.58	145.36	153.65	162.30	171.37	180.14	192.64	200.10	211.28	219.36	231.24
	74	.[b]										
	81	131.66	141.12	154.29	163.70	173.62	184.11	193.11	205.77	216.01	225.86	236.23
	92	132.96	140.77	148.04	157.89	167.37	177.75	183.83	196.01	202.76	210.67	219.83
	99	144.71	152.11	164.02	172.62	183.90	191.60	203.22	212.11	225.67	233.21	243.14
	110	136.86	147.07	155.34	163.40	175.38	182.19	193.54	201.18	209.31	222.95	229.12
	117	108.99	107.36	104.45	140.42	150.18	159.40	170.88	184.20	196.06	207.88	216.21
	128	147.44	157.10	165.98	175.70	187.00	197.04	208.44	216.43	229.20	237.64	246.56

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 3 of 10)

		Postnatal Day										
Group[a]	Animal ID	32	33	34	35	36	37	38	39	40	41	42
5	7	96.22	107.04	114.00	122.94	129.33	139.67	147.02	154.10	161.07	171.34	180.90
	21	138.66	149.43	160.18	168.13	180.32	188.60	200.56	213.26	222.03	232.11	240.32
	26	131.45	142.90	150.86	161.42	173.71	180.16	193.67	201.95	211.24	219.80	229.08
	39	128.61	138.48	147.39	154.56	168.35	175.60	185.38	192.51	204.11	210.22	219.60
	44	128.77	138.83	148.23	156.20	166.13	175.72	186.62	193.75	205.95	211.13	221.04
	57	134.02	142.68	150.47	159.66	171.38	180.12	190.86	201.42	207.24	214.62	226.45
	62	123.00	130.19	138.11	148.12	154.13	164.60	171.99	181.00	188.29	196.84	203.35
	75	128.01	140.22	147.80	155.78	165.55	175.79	183.10	192.07	202.92	208.20	219.44
	80	117.80	129.29	136.29	146.30	158.07	165.15	175.30	185.97	194.48	203.74	215.27
	93	130.60	141.45	150.76	160.77	169.35	177.44	187.88	198.22	206.48	216.03	227.36
	98	138.99	148.15	160.41	168.96	180.22	187.14	200.42	210.17	220.95	228.36	237.34
	111	138.56	147.61	158.12	169.00	179.54	191.91	204.13	213.29	222.71	233.90	240.55
	116	144.99	158.47	169.15	181.04	189.12	202.14	212.07	217.20	228.50	240.15	250.01
	129	148.75	159.33	171.43	180.43	193.06	200.74	209.90	220.24	233.42	238.60	251.02
	132	142.00	152.00	161.72	172.49	183.41	189.50	201.53	208.70	217.74	226.00	235.07
6	8	106.00	114.95	123.22	131.18	139.70	149.74	157.52	168.62	174.31	187.06	191.99
	11	107.13	116.20	126.79	133.48	143.89	152.74	160.37	171.50	177.20	188.36	197.16
	22	139.16	149.11	159.19	170.06	180.73	193.22	205.70	213.79	223.44	238.15	246.99
	25	122.07	130.10	136.43	145.58	153.85	161.77	171.07	176.55	182.77	189.87	198.55
	40	134.67	144.44	153.78	165.98	175.18	187.22	197.21	206.48	218.08	226.10	234.99
	43	124.54	133.30	142.02	150.95	160.18	171.41	181.48	181.99	195.60	204.15	211.97
	58	125.60	135.05	142.26	152.62	161.82	169.40	181.11	191.15	199.10	208.04	218.50
	61	143.25	152.66	161.14	169.70	180.53	193.04	201.01	209.75	222.28	229.10	240.71
	76	131.00	141.07	149.22	158.11	170.98	179.17	185.36	197.63	208.01	216.64	228.02
	79	.[b]										
	94	143.10	157.15	164.21	178.36	189.64	199.50	209.40	221.60	233.25	241.50	248.75
	97	132.08	145.00	154.27	163.89	173.41	183.89	193.56	202.40	211.64	218.88	229.45
	112	140.80	150.21	162.07	171.15	184.11	190.22	204.00	217.00	222.19	231.44	246.32
	115	.[b]										
	130	151.80	163.00	174.92	184.11	198.22	206.00	218.93	226.63	237.79	247.30	258.07

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 4 of 10)

Group[a]	Animal ID	Postnatal Day										
		32	33	34	35	36	37	38	39	40	41	42
7	9	102.99	112.47	121.16	129.22	139.93	145.96	155.02	164.73	172.50	185.05	193.82
	10	115.39	122.81	132.38	140.82	151.22	157.60	168.02	180.16	185.00	195.62	204.07
	23	126.60	137.79	146.50	156.07	164.84	171.25	182.95	189.40	199.45	210.28	217.33
	24	.[b]										
	41	124.48	134.83	142.47	152.02	159.98	172.10	183.17	191.54	203.03	212.51	217.53
	42	131.04	136.41	147.13	154.26	163.01	171.60	181.00	190.45	199.12	204.41	213.39
	59	126.11	133.25	147.10	155.82	166.75	176.00	186.59	193.44	203.34	210.78	220.14
	60	124.39	135.24	145.21	156.45	168.46	176.67	187.03	194.66	205.88	216.25	225.36
	77	123.10	133.04	139.65	151.44	158.69	168.35	173.72	178.87	191.04	199.92	207.24
	78	135.03	145.70	153.05	163.81	174.16	182.04	184.04	191.04	200.30	208.29	217.28
	95	132.64	142.53	149.08	161.51	168.52	179.04	189.41	198.62	208.37	217.95	225.22
	96	139.02	149.01	158.19	168.11	178.95	192.52	200.21	208.70	219.48	229.48	239.27
	113	135.01	141.98	150.87	162.74	171.28	182.59	195.35	205.23	217.41	229.32	234.56
	114	.[b]										
	131	.[b]										
8	2	101.50	107.74	115.51	122.19	131.27	138.32	146.31	155.91	160.27	169.35	176.97
	16	134.66	144.05	153.08	163.71	171.60	185.76	194.67	200.23	211.90	220.54	232.09
	31	105.13	101.14	97.31	97.15	137.46	144.52	154.95	166.05	177.11	184.56	197.76
	34	132.64	142.87	152.49	159.63	170.73	176.70	189.99	173.07	200.07	210.34	218.05
	49	136.19	145.93	153.05	163.28	172.76	184.23	192.46	203.60	209.40	.[e]	230.41
	52	142.99	151.55	161.39	171.19	181.66	192.11	202.03	217.60	222.95	228.69	247.58
	67	127.52	134.62	139.59	151.87	160.84	167.13	176.00	185.11	196.13	200.13	213.26
	70	137.11	148.53	157.46	170.47	180.30	187.06	197.94	206.54	215.68	220.92	233.78
	85	135.42	145.30	157.48	166.84	179.17	187.12	196.94	206.76	216.66	221.31	232.31
	88	136.54	145.29	151.57	162.31	170.91	181.34	190.28	198.16	205.17	213.01	223.70
	103	133.37	142.04	153.59	161.62	172.60	184.45	193.65	200.64	205.53	215.06	232.40
	106	139.40	148.52	157.98	169.23	177.26	185.10	197.81	202.00	209.09	220.22	225.94
	121	135.45	144.38	153.14	161.11	171.22	180.59	193.07	199.94	210.66	221.55	231.95
	124	138.58	148.81	157.01	164.59	175.26	183.71	192.46	200.05	208.17	217.90	222.07
	134	138.56	148.12	157.21	170.21	181.78	190.50	200.25	206.97	218.40	223.21	232.16

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 5 of 10)

Group[a]	Animal ID	Postnatal Day										
		32	33	34	35	36	37	38	39	40	41	42
9	3	101.42	108.13	117.63	121.11	128.60	138.03	144.12	151.50	155.06	165.40	171.10
	14	104.20	112.91	118.09	124.75	137.69	147.31	151.00	161.40	167.54	172.11	179.13
	17	.[b]										
	30	.[b]										
	35	128.55	138.72	149.86	159.16	169.40	176.81	187.76	194.26	206.84	211.21	219.57
	48	129.03	140.40	150.48	157.27	167.18	179.07	187.28	194.27	209.61	212.80	223.16
	53	130.80	140.01	147.58	155.66	167.54	175.18	187.20	192.77	204.32	209.55	220.00
	66	136.02	144.22	152.34	164.68	173.16	183.99	193.00	202.70	210.08	218.14	225.20
	71	141.35	148.88	160.17	169.18	181.12	191.90	199.31	207.60	217.38	226.17	234.78
	84	141.12	149.26	156.42	164.11	181.19	187.90	195.15	199.10	211.77	219.40	226.54
	89	139.38	149.30	156.38	163.42	178.10	187.66	197.98	201.84	213.60	222.22	229.52
	102	149.76	158.02	164.91	171.08	185.83	193.60	201.64	210.57	220.30	230.30	241.49
	107	146.32	154.55	165.14	172.91	186.81	197.46	206.99	208.00	218.30	220.18	236.16
	120	148.03	157.53	171.86	181.22	191.60	205.89	215.85	223.77	236.77	245.12	256.74
	125	138.92	150.59	159.15	169.14	183.00	192.58	198.71	209.56	219.26	226.81	232.29
10	136	107.26	115.51	123.48	129.98	138.62	148.37	156.40	163.77	172.02	183.16	187.58
	153	119.74	128.27	136.58	143.67	152.52	163.93	172.69	181.96	190.05	199.29	208.83
	154	129.79	139.16	148.50	158.47	168.55	181.50	190.90	200.52	211.92	219.16	226.95
	171	126.77	137.36	148.18	153.55	163.07	175.12	184.49	192.22	199.42	212.35	223.72
	172	136.67	145.77	153.68	162.00	169.80	181.91	189.97	198.80	207.50	218.76	223.81
	182	149.39	157.58	169.00	180.88	192.90	204.51	215.62	227.87	239.12	246.52	259.10
	199	134.36	141.98	156.62	154.47	169.71	178.02	187.97	200.07	209.24	215.51	229.46
	200	140.40	151.96	159.75	172.37	180.33	192.20	203.97	210.10	220.87	227.34	237.86
	217	.[g]										
	218	132.48	142.55	150.43	160.46	168.76	175.67	185.14	193.38	202.42	208.22	215.75
	235	147.81	158.12	167.48	178.31	191.48	200.38	212.62	216.30	223.60	231.00	241.64
	236	140.13	148.84	159.02	171.30	180.67	190.63	203.09	210.85	219.50	228.42	237.41
	253	130.25	140.57	147.57	157.00	166.07	175.85	186.48	195.63	204.81	207.72	223.14
	254	145.65	154.19	161.61	171.80	178.37	189.90	198.93	207.37	217.51	224.37	233.00
	270	148.68	158.59	169.55	179.34	190.23	199.52	210.18	219.01	228.98	237.18	245.26

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 6 of 10)

		Postnatal Day										
Group[a]	Animal ID	32	33	34	35	36	37	38	39	40	41	42
11	137	121.59	129.16	138.56	145.32	151.44	162.09	168.68	177.24	177.25	190.97	191.62
	152	128.51	135.92	147.89	151.16	165.29	171.61	180.79	192.47	203.45	212.28	217.48
	155	137.41	146.11	158.68	166.76	178.56	185.79	196.78	207.97	216.40	226.95	230.49
	170	135.69	145.24	155.71	164.20	174.14	184.22	194.06	202.83	212.50	219.31	224.64
	173	147.35	156.65	167.79	180.77	191.72	203.95	218.66	223.72	236.04	247.78	257.99
	183	124.72	133.26	139.42	152.92	162.33	171.87	180.40	192.84	202.30	206.37	215.10
	198	138.05	147.51	156.12	165.10	177.32	188.95	198.66	205.77	216.00	224.83	231.98
	201	136.59	147.09	153.96	166.05	173.88	185.08	198.11	208.07	216.59	223.34	233.17
	216	136.62	147.56	154.11	165.52	175.52	189.86	197.22	208.25	227.80	225.57	238.19
	219	137.77	145.71	154.14	164.52	172.98	184.52	193.19	200.90	212.01	217.60	226.60
	234	136.41	146.60	154.07	164.81	168.85	179.49	188.47	196.91	203.18	212.72	219.03
	237	141.31	150.28	160.37	168.15	182.44	189.65	200.47	209.05	219.40	227.52	237.43
	252	151.33	160.09	170.48	178.83	190.48	199.95	212.48	222.62	231.72	239.12	249.75
	255	144.05	152.15	161.92	171.36	181.85	192.16	200.66	210.06	221.36	227.79	234.66
	269	145.76	156.06	165.13	179.31	187.02	198.54	210.95	221.27	228.47	234.74	245.72
12	138	105.93	110.26	113.44	117.19	118.96	123.96	126.48	126.92	127.06	129.77	131.93
	151	108.79	111.07	114.03	117.75	120.91	124.58	126.08	128.67	128.72	132.52	131.16
	156	117.22	123.28	127.48	129.57	137.21	143.45	145.21	145.90	150.20	152.76	153.67
	169	130.37	136.75	141.29	149.02	151.46	156.41	162.29	165.22	170.28	170.69	171.95
	174	143.44	147.68	155.66	158.23	163.09	167.85	170.91	173.03	176.60	179.34	179.90
	184	126.89	132.77	133.82	139.56	143.00	144.13	147.16	149.00	151.21	150.82	151.25
	197	123.09	127.76	133.54	140.00	143.37	147.70	152.40	156.39	159.76	160.38	162.05
	202	128.99	133.66	138.50	145.03	148.92	150.32	156.31	157.49	158.02	157.54	159.99
	215	137.12	143.26	147.50	154.44	160.75	165.78	171.90	173.29	180.51	178.90	182.81
	220	133.75	141.60	146.24	150.84	156.04	160.83	162.31	167.50	170.99	171.88	174.84
	233	137.49	143.90	147.31	152.86	158.12	161.75	163.85	168.61	169.11	170.96	173.00
	238	139.69	146.75	148.38	155.63	162.53	163.26	168.50	169.21	172.86	173.38	176.16
	251	127.32	135.18	140.57	146.50	152.87	158.19	161.14	164.84	167.82	166.89	168.79
	256	138.46	146.32	153.22	160.00	165.37	168.77	175.28	178.04	183.15	182.43	184.71
	268	133.67	140.77	143.81	149.35	153.22	157.97	160.77	166.47	167.29	167.00	170.42

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 7 of 10)

		Postnatal Day										
Group[a]	Animal ID	32	33	34	35	36	37	38	39	40	41	42
13	141	114.65	123.60	134.13	129.16	142.47	151.91	163.31	158.64	163.11	168.21	177.15
	148	130.96	141.73	150.40	162.52	170.70	183.54	193.19	203.04	211.06	221.16	232.70
	159	119.32	125.23	133.75	140.71	151.99	160.13	169.15	178.49	184.50	191.49	198.83
	166	133.46	142.88	154.09	162.35	171.85	177.78	191.60	201.29	211.28	218.10	222.72
	177	144.80	155.68	167.52	177.24	188.71	201.04	212.72	220.39	231.40	242.80	251.79
	187	132.19	141.32	149.54	159.90	167.56	177.44	184.13	193.19	202.59	210.83	220.70
	194	120.30	126.58	133.40	143.26	154.09	165.24	172.22	180.52	187.83	198.77	206.43
	205	133.91	144.70	153.92	165.68	175.35	182.46	192.44	204.79	214.57	223.38	231.96
	212	138.82	149.58	155.57	167.38	178.33	191.42	199.98	208.75	216.97	223.62	234.68
	223	138.54	143.59	150.00	170.17	175.53	186.59	194.99	200.31	209.88	215.16	227.93
	230	127.20	135.86	145.57	154.70	163.72	174.47	181.43	190.07	198.52	204.71	210.00
	241	145.44	155.70	163.71	178.58	187.73	204.66	214.82	225.12	233.89	237.51	248.75
	248	131.25	141.87	151.12	160.22	167.95	178.58	187.74	195.03	202.74	213.66	221.97
	259	146.42	154.94	164.11	176.13	184.09	193.27	205.27	210.24	218.55	225.33	234.61
	265	148.81	156.92	164.31	176.63	189.44	200.61	211.31	219.37	229.02	231.41	245.99
14	142	113.13	116.14	125.85	135.16	145.21	154.22	162.35	170.68	177.25	184.83	193.80
	147	117.65	127.77	135.83	142.94	150.35	160.24	166.36	174.75	183.57	191.65	198.95
	160	117.42	124.40	133.78	141.23	152.47	160.74	168.31	179.31	190.36	194.98	200.98
	165	114.55	120.66	128.97	135.49	147.17	153.38	166.19	172.99	180.23	190.14	197.76
	178	135.33	145.42	153.89	163.12	175.30	183.93	192.74	197.96	209.30	216.55	224.58
	188	125.18	133.72	141.45	149.12	157.65	167.58	176.61	185.20	192.64	199.77	209.23
	193	128.51	137.29	145.82	154.82	164.82	173.77	181.97	190.50	197.66	207.60	213.58
	206	131.91	144.56	150.34	159.80	168.07	180.69	191.51	200.55	206.78	213.10	224.02
	211	128.36	138.82	142.56	155.23	161.11	171.67	178.29	184.37	192.90	195.34	206.51
	224	129.42	136.88	143.38	151.73	163.72	172.44	179.89	191.65	201.91	203.15	212.46
	229	134.09	148.65	159.14	167.73	176.74	189.80	195.30	203.65	212.21	220.08	232.03
	242	135.27	144.28	149.49	163.24	170.74	.[h]					
	247	142.08	152.04	158.04	169.54	179.99	187.05	197.19	209.91	216.73	225.98	232.41
	260	135.56	149.57	158.03	169.93	180.46	192.98	202.07	214.23	221.82	230.06	243.32
	264	143.18	154.38	161.29	175.30	183.64	196.34	205.94	213.38	222.33	230.13	242.67

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 8 of 10)

		Postnatal Day										
Group[a]	Animal ID	32	33	34	35	36	37	38	39	40	41	42
15	139	114.92	123.23	131.81	140.76	151.55	161.58	170.58	178.13	187.41	193.11	202.70
	150	116.75	122.80	130.52	140.88	148.85	157.44	167.48	175.84	185.71	195.73	196.96
	157	113.40	120.63	129.23	137.52	147.60	155.49	164.15	175.49	182.48	190.63	200.35
	168	127.20	135.56	144.43	151.01	162.33	170.48	180.15	188.17	194.85	201.47	213.32
	175	124.37	132.14	142.19	147.76	158.49	167.18	174.91	182.98	192.95	201.48	206.81
	185	124.70	133.96	142.71	152.23	160.00	170.49	175.72	187.07	195.03	205.11	209.36
	196	132.84	140.35	135.26	148.22	157.23	169.74	177.48	186.28	196.95	202.18	215.90
	203	125.27	135.04	145.05	154.92	164.38	173.65	183.38	191.36	201.57	207.56	215.00
	214	118.23	123.65	130.80	140.85	148.58	158.59	165.87	172.75	181.37	188.29	196.60
	221	128.42	139.14	148.25	160.38	170.27	181.38	189.38	194.64	204.15	216.30	226.92
	232	124.73	133.87	137.76	148.32	156.73	165.14	172.44	180.12	191.97	196.98	205.89
	239	135.23	143.65	151.95	160.22	168.69	178.47	186.65	199.97	206.21	216.58	226.45
	250	128.60	137.87	144.17	154.81	162.98	172.85	182.77	190.96	199.44	206.60	213.11
	257	142.78	152.45	161.82	171.10	182.00	196.67	204.46	215.73	227.32	236.33	245.47
	267	134.54	142.21	153.94	165.04	176.72	184.07	195.03	203.93	212.81	221.72	231.22
16	140	110.29	119.40	125.49	136.15	145.62	153.35	162.33	167.60	177.16	186.14	194.25
	149	104.52	111.86	118.60	127.71	134.00	143.26	149.58	154.66	159.80	166.31	163.70
	158	117.61	123.79	127.48	136.52	147.74	156.40	164.16	170.08	174.20	184.90	192.24
	167	100.99	108.15	113.45	121.85	128.34	136.74	144.76	151.45	155.54	163.23	172.38
	176	125.77	132.15	141.73	151.61	161.34	176.08	179.25	191.09	200.33	208.86	221.23
	186	120.75	129.09	133.51	144.49	151.14	163.99	170.61	180.22	184.01	190.69	196.67
	195	125.26	132.35	139.45	147.57	157.81	168.24	174.75	182.16	187.36	194.42	198.15
	204	111.60	118.02	124.77	135.85	142.21	150.20	155.20	162.16	168.22	174.94	183.15
	213	113.54	120.27	125.91	136.92	145.26	153.43	160.38	170.31	180.36	182.51	195.31
	222	121.40	130.10	134.61	147.04	156.00	167.12	170.74	178.97	187.10	195.73	204.10
	231	109.27	117.60	122.08	130.28	140.48	147.66	153.48	162.11	169.22	175.58	181.02
	240	126.68	136.68	142.80	152.24	164.40	171.73	180.48	192.01	196.97	206.76	218.19
	249	122.87	129.66	136.41	147.61	155.00	165.68	174.76	182.30	189.11	193.37	205.90
	258	136.74	147.50	154.67	166.76	174.09	188.22	192.50	203.45	210.58	217.74	226.57
	266	131.69	140.27	149.90	160.21	176.76	181.29	191.12	201.40	205.27	215.42	223.09

(continued)

Table A-3. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 32 Through 42 (page 9 of 10)

Group[a]	Animal ID	Postnatal Day										
		32	33	34	35	36	37	38	39	40	41	42
17	143	114.14	122.56	131.66	138.47	150.84	159.53	166.51	179.34	185.80	196.13	199.66
	146	121.26	125.43	135.89	145.24	155.14	164.78	174.35	185.45	196.36	206.12	211.58
	161	126.23	133.01	141.79	149.04	160.40	171.67	181.58	190.60	200.40	211.62	215.78
	164	142.55	150.39	157.43	168.57	182.88	194.22	201.77	214.83	224.20	234.98	245.79
	179	149.93	158.57	167.83	181.40	190.21	200.31	208.60	216.27	229.70	237.55	248.22
	189	126.40	137.16	144.51	155.94	166.03	175.46	184.90	192.82	203.76	211.08	219.92
	192	147.19	151.29	166.83	175.20	188.17	197.57	212.69	219.83	232.05	240.06	250.22
	207	133.29	142.23	149.66	159.34	166.39	178.93	189.07	197.92	205.58	208.67	219.91
	210	118.59	126.86	134.59	143.43	152.75	161.38	172.87	180.12	188.94	193.97	204.99
	225	142.07	152.20	160.58	171.84	180.15	193.00	204.17	215.40	222.31	234.62	250.25
	228	132.43	141.36	152.00	161.96	169.12	180.34	190.69	200.99	208.02	213.25	227.03
	243	144.17	153.75	161.08	174.68	185.66	201.28	207.15	224.01	232.75	245.33	265.69
	246	127.86	138.28	146.06	154.09	160.87	169.72	178.19	186.56	194.76	200.14	209.81
	261	131.71	141.84	149.21	159.26	168.55	177.86	186.92	195.25	203.99	212.12	222.57
	263	139.49	150.29	156.17	166.06	175.51	184.07	193.91	202.44	210.63	216.92	223.37
18	144	110.52	116.45	125.63	133.51	145.40	153.37	159.71	163.63	170.22	177.58	184.72
	145	118.32	128.05	135.10	143.04	152.84	162.55	173.15	185.21	195.78	205.42	214.47
	162	114.53	120.00	126.54	135.45	143.68	153.51	161.21	171.34	180.25	187.15	196.50
	163	127.81	137.33	142.13	156.20	166.15	176.78	184.87	197.56	207.41	218.50	229.66
	180	127.33	133.07	141.87	151.17	160.45	166.42	176.08	186.40	195.90	197.98	206.64
	181	116.32	122.08	129.94	138.26	145.87	150.41	159.00	165.53	176.91	185.06	190.55
	190	124.75	132.91	138.65	147.46	157.36	166.37	174.79	182.26	189.93	193.14	202.39
	191	121.97	130.45	138.08	147.14	156.81	165.47	173.68	179.62	189.75	196.65	202.46
	208	130.03	140.28	149.60	159.54	165.28	171.49	182.72	188.82	197.31	202.25	213.20
	209	137.10	146.95	159.38	167.94	180.35	187.89	197.00	207.20	219.27	224.11	236.52
	226	141.31	154.51	164.55	176.85	184.70	195.21	203.26	214.44	229.19	237.27	248.00
	227	134.84	144.10	154.32	165.83	175.81	183.86	197.40	204.99	219.84	220.44	234.40
	244	140.62	150.46	161.31	169.86	179.49	192.33	204.18	211.09	224.74	231.72	241.62
	245	133.04	142.44	147.89	158.30	170.32	179.78	188.75	194.75	208.61	216.09	227.10
	262	121.01	129.98	139.22	147.63	155.73	164.42	171.62	180.83	190.04	199.12	210.74

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.
[b]Male was removed from the study because his correct postnatal day 0 could not be confirmed.
[c]Male was removed from the study because it was not dosed on the correct postnatal days.
[d]Male was found dead on postnatal day 37 after dosing (misdirected dose).
[e]Body weight inadvertently not recorded.
[f]Male was euthanized on postnatal day 29 after dosing due to a leg injury.
[g]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).
[h]Male was found dead on postnatal day 37 prior to dosing (misdirected dose).

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 1 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
1	1	209.27	220.42	232.42	239.03	245.70	254.95	267.85	275.23	282.90	290.31	
	15	216.61	225.62	236.10	240.92	250.71	263.11	269.74	280.43	283.45	293.56	
	32	230.46	238.60	250.02	250.58	260.87	270.95	277.81	285.73	288.82	300.05	
	33	223.55	235.03	242.73	243.95	257.93	267.41	275.18	295.88	293.71	312.83	
	50	241.37	250.87	261.50	267.13	272.76	282.16	294.18	302.38	305.90	320.45	
	51	225.36	235.80	244.70	252.08	264.47	270.36	277.06	291.26	294.84	307.18	
	68	238.47	251.23	262.11	273.17	282.29	290.37	300.16	310.47	318.00	326.72	
	69	.[c]										
	86	.[c]										
	87	267.85	275.90	285.71	291.71	299.96	309.99	322.11	332.60	340.14	348.74	358.34
	104	261.80	274.83	283.75	287.31	297.63	308.15	316.91	328.84	333.15	339.05	349.01
	105	251.48	262.12	268.14	279.82	291.09	294.03	301.78	312.00	324.86	332.66	341.00
	122	234.16	243.62	251.60	259.17	269.16	273.50	285.16	289.42	296.15	304.66	316.19
	123	227.38	233.27	243.64	254.36	263.78	270.18	274.50	284.75	294.78	302.30	309.18
	135	.[c]										
2	4	191.47	194.82	202.99	209.45	217.60	227.99	234.16	241.60	246.40	256.18	
	18	.[d]										
	29	211.58	217.02	225.68	231.67	241.51	248.16	256.43	262.25	273.11	275.98	
	36	217.66	230.61	237.55	242.40	250.00	263.18	271.16	278.08	285.26	290.08	
	47	212.22	220.40	223.79	232.78	236.95	246.11	251.61	255.86	260.70	264.61	
	54	.[e]										
	65	220.03	227.40	238.27	244.49	257.45	260.24	271.11	281.20	286.02	293.77	
	72	222.87	233.59	243.62	249.43	259.63	269.11	280.31	287.63	299.06	303.89	
	83	212.77	222.65	225.12	233.21	240.62	250.11	258.72	265.56	256.74	264.39	270.77
	90	213.52	221.41	228.41	238.45	247.82	252.12	265.89	271.89	277.46	284.80	291.54
	101	226.23	232.94	242.37	248.70	255.57	264.64	273.16	280.74	290.00	295.34	299.05
	108	221.85	229.11	236.25	238.83	247.69	254.19	263.11	271.50	276.59	286.32	280.48
	119	.[c]										
	126	216.76	223.16	229.36	235.89	242.60	245.14	256.73	262.47	268.84	275.21	275.28
	133	227.28	234.55	240.83	246.71	260.27	266.13	267.44	285.46	287.82	295.10	297.03

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 2 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
3	5	175.91	179.46	187.11	197.06	198.45	206.93	211.03	219.41	225.04	234.62	
	13	188.02	195.05	201.64	209.86	218.73	222.39	230.16	237.21	239.81	249.76	
	19	207.42	215.13	222.29	222.40	231.97	239.18	248.01	259.48	263.28	269.32	
	28	203.80	212.26	219.97	222.70	230.05	233.69	243.61	248.00	255.75	266.60	
	37	200.03	207.79	211.69	216.13	226.08	225.31	233.94	244.90	251.93	257.16	
	46	199.71	208.72	214.04	218.76	224.49	235.20	241.17	246.32	257.13	259.83	
	55	.[c]										
	64	209.36	216.04	220.29	228.33	229.74	242.11	248.61	256.13	262.94	268.71	
	73	209.16	218.05	227.35	227.57	235.99	243.18	251.73	262.30	265.66	269.52	
	82	211.44	217.46	223.57	228.23	234.67	244.18	251.57	255.94	265.05	266.75	276.80
	91	211.63	220.15	225.19	236.41	246.12	251.24	261.15	268.46	279.73	286.50	292.36
	100	201.52	212.20	220.91	225.34	232.52	238.16	246.12	250.10	259.84	262.06	272.55
	109	195.12	201.24	208.38	214.63	216.19	225.16	231.24	236.21	240.01	239.36	249.00
	118	.[c]										
	127	.[c]										
4	6	186.06	193.57	200.66	208.39	216.42	224.48	236.11	240.16	247.32	250.88	
	12	198.50	206.91	217.86	225.26	237.97	244.06	252.16	256.12	262.79	277.32	
	20	.[f]										
	27	238.12	248.10	257.75	268.08	275.13	287.16	297.21	304.81	317.36	330.07	
	38	242.59	250.11	261.27	268.83	282.98	285.16	301.21	307.90	313.09	323.50	
	45	232.56	237.86	251.15	258.99	264.90	280.75	286.21	299.39	305.87	315.68	
	56	248.40	257.18	267.73	273.13	282.18	292.14	302.40	315.82	320.28	344.12	
	63	237.30	246.75	257.69	267.67	272.25	281.16	291.61	302.18	311.58	317.22	
	74	.[c]										
	81	246.86	255.15	263.05	271.26	281.68	290.76	296.12	309.33	314.89	326.77	332.24
	92	228.42	233.40	243.85	252.01	262.77	267.48	276.12	283.47	287.93	297.80	303.74
	99	253.66	262.46	270.41	282.29	295.52	300.59	311.48	326.44	329.52	341.65	352.23
	110	240.91	251.70	261.56	267.38	275.55	286.60	297.63	301.84	306.53	312.80	330.00
	117	231.16	239.12	248.83	258.31	267.89	275.28	285.01	297.15	304.26	311.50	321.40
	128	256.08	265.57	278.86	288.03	298.70	309.18	319.26	330.63	333.98	342.17	356.30

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 3 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
5	7	187.53	196.30	202.55	215.83	215.63	228.92	240.96	243.16	256.32	222.96	
	21	252.66	259.20	273.88	282.14	290.53	300.28	312.02	320.37	325.75	325.81	
	26	238.71	243.43	257.09	266.69	283.77	288.33	297.43	310.39	313.82	329.55	
	39	231.50	237.78	244.92	255.84	263.33	273.14	283.86	286.60	293.39	302.16	
	44	233.11	237.11	246.62	255.17	266.86	274.89	286.11	298.03	304.21	307.23	
	57	235.77	239.62	250.55	261.91	272.11	278.75	292.22	298.26	303.63	316.25	
	62	210.05	219.35	226.68	235.63	244.66	252.86	260.28	269.78	274.90	280.11	
	75	226.30	233.15	244.02	249.88	259.22	266.23	275.21	284.57	292.79	299.36	
	80	223.90	234.26	242.03	253.25	261.92	274.71	280.11	290.68	300.96	307.01	318.19
	93	237.56	242.29	252.32	263.06	275.37	278.69	290.01	300.71	309.01	319.31	335.81
	98	245.44	253.44	260.87	269.09	280.98	284.19	296.90	305.68	315.17	317.62	327.03
	111	247.02	254.45	267.84	276.10	286.07	293.72	303.16	315.40	318.74	330.80	338.28
	116	259.31	269.47	279.39	286.36	296.80	307.68	320.14	326.75	336.82	344.51	356.71
	129	257.97	262.92	275.09	278.56	294.53	300.03	311.43	322.18	331.32	339.04	356.40
	132	245.12	253.44	259.38	268.68	276.58	285.99	295.85	301.11	306.15	318.80	327.05
6	8	203.15	211.31	219.24	232.04	238.67	247.40	259.05	266.17	273.26	284.20	
	11	205.63	215.98	224.36	233.09	236.38	251.79	257.18	266.74	276.66	280.65	
	22	260.22	267.38	283.90	289.72	301.20	312.64	326.11	342.88	351.43	366.80	
	25	207.34	214.62	224.42	233.92	241.47	252.61	261.21	273.73	276.99	287.55	
	40	246.32	259.39	270.16	278.72	290.88	300.92	312.68	319.12	326.35	344.56	
	43	219.00	227.08	235.96	242.47	249.01	257.07	266.21	274.50	276.50	290.02	
	58	228.66	235.56	242.15	247.17	259.10	270.24	277.16	285.72	291.01	301.40	
	61	247.43	258.84	266.63	272.19	283.31	293.41	302.01	315.72	317.13	329.24	
	76	237.07	243.19	248.87	258.27	267.33	273.09	283.16	296.18	303.02	307.80	332.33
	79	.[c]										
	94	263.64	270.81	280.61	291.56	294.36	310.02	319.11	326.08	333.95	347.74	362.92
	97	239.87	248.84	261.91	270.29	282.02	293.54	301.92	310.18	318.76	329.04	345.43
	112	253.37	264.50	275.07	288.35	297.61	310.97	321.48	332.38	335.93	354.04	358.56
	115	.[c]										
	130	265.60	277.67	288.74	294.09	306.77	320.95	326.11	336.35	350.61	362.02	371.02

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 4 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
7	9	202.80	213.02	221.36	230.09	232.93	245.25	254.60	261.84	269.51	279.41	
	10	214.10	224.69	230.18	241.45	248.92	261.06	268.51	278.45	288.53	297.82	
	23	225.64	233.21	245.71	252.90	264.96	272.68	283.16	288.64	289.58	310.31	
	24	.[c]										
	41	224.50	235.17	243.70	252.39	262.32	269.55	276.22	285.79	291.75	305.23	
	42	222.01	229.66	240.01	245.99	254.77	261.29	273.02	279.31	284.01	297.86	
	59	231.18	235.02	248.54	250.44	258.30	270.20	280.45	288.00	289.04	300.60	
	60	233.28	241.15	250.26	256.29	267.19	276.21	284.01	298.21	307.30	316.21	
	77	218.11	227.88	233.87	216.77	244.52	254.35	263.91	273.47	277.56	288.56	294.07
	78	225.02	235.19	243.94	248.04	259.64	269.89	281.16	287.10	296.77	302.12	317.40
	95	233.03	240.79	250.03	256.95	267.24	276.13	285.11	292.78	300.91	310.10	317.36
	96	251.09	261.72	269.64	275.67	290.92	300.65	315.02	322.53	330.60	340.11	352.25
	113	247.23	255.71	263.75	271.50	283.57	292.70	300.64	308.98	320.03	332.16	342.29
	114	.[c]										
	131	.[c]										
8	2	183.25	191.86	200.05	209.30	213.00	221.48	230.15	238.92	247.04	255.61	
	16	239.90	251.27	260.03	267.46	276.62	286.15	299.01	305.63	308.83	322.13	
	31	206.90	212.87	222.20	227.51	238.66	250.11	261.01	270.55	279.19	292.14	
	34	222.70	228.54	238.21	248.75	254.98	264.21	272.18	283.10	289.27	300.25	
	49	236.82	249.07	257.72	266.49	278.03	284.05	295.15	298.57	304.47	307.71	
	52	250.21	261.73	269.65	271.36	285.48	287.16	300.95	305.87	317.18	327.70	
	67	215.04	219.01	228.11	229.05	238.46	244.16	252.18	257.23	263.35	270.81	
	70	238.84	249.23	258.46	267.12	275.60	284.01	294.84	302.40	311.03	314.80	
	85	238.64	248.56	256.51	269.04	278.60	289.23	299.03	308.97	308.26	316.42	334.50
	88	227.30	237.11	246.04	252.25	263.12	267.05	275.31	284.24	287.81	295.02	301.54
	103	234.11	238.10	253.83	260.32	263.34	274.16	280.95	289.33	300.27	303.46	311.85
	106	234.04	245.20	254.26	260.72	268.06	278.15	284.11	292.48	293.20	303.26	311.31
	121	239.14	245.92	259.18	266.11	277.99	287.31	296.16	302.83	304.10	315.02	327.16
	124	232.02	244.45	252.41	253.57	262.16	268.50	278.44	290.40	293.55	301.45	315.90
	134	238.34	249.59	258.66	266.24	277.78	285.14	292.21	301.24	299.44	314.60	327.36

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 5 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
9	3	174.76	180.04	194.42	198.13	208.03	209.25	216.41	229.49	231.73	237.30	
	14	184.43	195.35	200.70	207.65	216.57	221.72	227.18	230.91	243.99	248.72	
	17	.[c]										
	30	.[c]										
	35	225.52	236.41	246.51	255.04	263.03	274.98	285.16	284.58	289.46	298.60	
	48	233.86	235.44	244.71	255.70	265.10	273.18	280.17	287.71	284.02	294.12	
	53	228.00	238.60	247.04	254.35	262.10	275.26	285.41	291.26	288.71	297.40	
	66	232.87	241.17	249.87	258.84	266.67	275.63	284.16	295.83	292.42	302.91	
	71	238.43	246.95	256.30	262.83	274.66	280.16	291.61	295.77	296.20	305.00	
	84	233.37	241.12	247.42	255.18	267.58	275.11	281.23	287.57	290.80	299.01	307.85
	89	240.00	246.40	256.48	257.31	268.95	277.54	283.91	293.41	298.27	300.58	315.65
	102	250.37	256.56	261.91	272.70	280.73	293.31	302.13	311.86	315.42	322.16	342.08
	107	243.36	251.50	256.62	260.12	272.09	283.02	292.16	302.84	306.40	309.75	320.11
	120	264.94	275.47	287.00	295.38	302.23	311.23	323.16	334.60	342.04	349.66	359.56
	125	240.46	248.90	258.68	266.37	275.41	281.49	290.61	301.34	296.28	307.88	322.79
10	136	197.07	204.00	214.57	219.46	229.94	236.15	246.00	255.87	259.66	270.90	
	153	214.17	224.03	232.66	245.04	252.78	261.65	268.07	279.00	289.63	301.13	
	154	240.10	248.81	260.36	269.00	281.36	288.49	300.83	307.42	321.77	331.98	
	171	228.86	242.31	251.36	259.97	266.68	279.91	287.56	297.63	310.34	320.71	
	172	235.13	241.03	250.09	258.83	271.17	277.58	287.38	292.38	304.50	316.88	
	182	269.53	282.79	292.63	306.99	315.20	328.63	341.67	356.40	364.40	375.68	
	199	229.27	234.37	247.80	256.29	262.52	274.65	286.98	294.10	301.49	317.20	
	200	248.34	259.69	266.85	280.57	287.28	294.96	308.42	321.05	329.88	339.10	
	217	.[g]										
	218	223.48	229.75	238.58	246.42	254.73	263.10	269.87	277.44	285.78	293.03	
	235	254.00	262.50	273.21	283.61	291.91	300.41	310.78	319.42	328.49	339.16	349.07
	236	243.51	253.89	265.93	273.77	280.83	290.26	297.83	306.71	314.35	324.38	336.70
	253	231.00	237.89	246.42	254.50	264.91	271.17	281.48	292.47	301.18	309.71	311.74
	254	242.07	248.70	257.35	268.26	278.58	286.41	295.37	302.20	311.86	319.96	331.13
	270	255.02	261.76	271.37	284.75	291.94	302.62	309.57	324.29	328.98	341.39	353.57

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 6 of 10)

Group[a]	Animal ID	Postnatal Day										
		43	44	45	46	47	48	49	50	51	52	53[b]
11	137	198.79	205.55	212.66	216.64	221.85	223.37	224.52	232.25	234.44	238.72	
	152	224.34	231.70	240.37	250.21	255.70	265.86	273.51	277.29	282.12	288.94	
	155	239.25	247.06	254.69	263.00	269.45	274.40	274.87	280.84	287.64	290.80	
	170	232.79	237.66	247.49	256.52	260.09	267.11	269.29	274.41	279.33	284.54	
	173	271.02	280.95	290.31	301.05	308.69	315.09	331.24	338.51	349.29	356.86	
	183	224.88	233.81	244.55	248.72	257.27	263.50	270.75	279.08	285.44	290.86	
	198	241.59	248.90	261.40	271.35	279.53	288.22	294.91	301.40	310.14	314.50	
	201	241.67	248.65	255.01	265.53	270.36	276.20	283.20	290.33	297.77	301.69	
	216	248.56	259.30	266.67	274.20	285.72	292.18	302.40	314.14	320.40	328.90	
	219	232.98	237.38	240.92	245.92	250.02	253.49	253.92	251.24	258.84	260.21	
	234	225.55	234.85	242.35	251.19	257.82	263.40	270.58	278.44	288.22	292.64	300.78
	237	246.73	254.69	260.53	266.33	273.49	278.09	283.06	285.88	290.15	292.11	294.50
	252	258.08	263.90	273.03	278.09	284.33	288.87	293.41	295.04	297.95	299.87	303.35
	255	243.37	251.89	258.70	265.84	270.60	274.66	277.07	285.57	286.46	289.84	291.88
	269	258.23	263.24	272.78	284.57	292.24	298.22	309.87	315.97	326.37	327.75	331.45
12	138	135.80	135.94	136.23	138.98	139.48	139.53	139.76	143.15	143.07	144.60	
	151	132.21	133.78	135.35	136.24	136.58	137.39	137.80	139.91	140.71	140.36	
	156	154.24	154.55	157.85	159.76	158.77	160.07	161.20	162.32	158.08	162.80	
	169	173.28	175.67	176.96	175.42	177.94	177.98	178.91	182.29	181.56	181.23	
	174	179.52	179.33	179.97	178.38	178.94	180.57	178.14	174.90	174.72	176.78	
	184	153.27	153.07	152.35	155.00	155.78	154.50	157.48	157.94	158.58	156.78	
	197	162.88	165.75	165.36	166.53	169.08	170.51	168.20	169.64	171.37	173.06	
	202	160.75	159.50	162.17	163.75	164.66	163.17	163.58	165.48	164.92	166.25	
	215	185.10	185.76	186.03	185.96	188.93	188.27	188.25	190.19	193.26	194.12	
	220	173.91	174.85	178.03	176.83	178.73	176.90	177.59	180.77	178.38	178.93	
	233	172.35	172.38	173.75	173.19	176.60	175.07	176.60	174.66	176.75	176.61	177.40
	238	177.11	177.29	179.41	180.09	178.32	181.10	181.81	183.89	183.81	185.43	184.30
	251	174.86	174.91	175.42	177.28	179.18	178.60	180.35	182.52	186.54	185.35	185.24
	256	188.01	188.63	190.00	189.91	190.99	189.64	189.76	192.65	193.48	194.14	193.62
	268	171.64	173.04	172.00	174.32	170.92	171.80	173.88	.[h]			

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 7 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
13	141	187.99	194.14	204.59	212.16	221.82	233.52	243.35	248.80	261.68	274.52	
	148	242.82	251.86	261.38	271.22	280.86	289.66	301.19	314.16	322.77	336.97	
	159	206.29	216.81	221.90	231.64	240.78	248.34	256.69	264.09	277.90	286.24	
	166	234.39	244.51	249.81	262.09	271.32	279.43	287.76	303.49	307.21	316.13	
	177	263.55	274.57	282.58	294.29	304.34	311.00	325.75	330.90	344.40	354.86	
	187	227.22	236.71	244.34	253.29	260.25	271.32	280.89	288.44	300.92	307.34	
	194	214.36	224.86	233.92	242.28	249.81	256.20	267.05	272.76	281.90	293.88	
	205	243.60	250.26	258.51	271.50	281.13	292.03	297.45	311.06	325.43	336.30	
	212	242.10	248.17	261.21	267.64	277.88	285.67	298.08	306.58	317.57	328.05	
	223	237.40	243.74	252.51	258.72	270.15	282.19	287.85	300.65	309.70	355.23	
	230	218.63	229.74	241.42	244.06	257.65	261.58	272.13	284.08	291.81	298.17	310.21
	241	260.55	267.87	272.08	284.66	296.18	298.33	309.53	318.96	327.18	342.82	353.57
	248	231.30	242.61	252.17	262.13	272.00	279.52	292.67	301.68	313.06	327.24	338.26
	259	243.38	251.63	262.27	269.31	275.36	281.66	293.12	302.49	311.87	321.99	329.37
	265	251.99	263.41	270.36	282.06	293.46	299.10	312.49	323.07	334.92	344.54	355.77
14	142	199.99	208.45	216.26	225.75	230.78	236.35	240.73	251.02	259.92	266.84	
	147	205.90	211.73	223.03	229.79	231.69	245.92	250.42	257.99	268.30	277.11	
	160	206.45	220.04	225.78	234.18	240.61	247.18	259.90	267.13	277.44	284.81	
	165	205.04	214.02	224.36	229.61	239.96	247.72	253.32	266.68	271.59	280.64	
	178	233.63	243.57	250.10	261.18	272.72	278.63	291.04	302.20	308.75	324.18	
	188	215.70	224.64	235.50	242.29	249.47	256.68	263.36	275.34	282.88	293.72	
	193	225.18	230.79	238.14	246.57	257.65	262.39	269.16	280.95	289.46	299.09	
	206	230.67	238.71	243.11	244.78	259.59	266.94	277.61	287.60	296.97	307.70	
	211	216.12	223.71	230.13	236.24	251.87	255.75	263.33	276.52	288.42	293.53	
	224	221.29	229.55	231.79	240.66	250.29	252.23	261.54	271.71	283.14	284.60	
	229	244.49	252.20	258.31	264.85	280.10	284.72	292.37	302.40	318.13	329.43	328.71
	242	.[i]										
	247	245.95	253.42	262.68	272.43	280.22	292.71	306.52	314.03	321.11	333.18	341.71
	260	253.59	260.22	272.65	281.61	290.19	294.51	308.91	315.58	329.75	340.72	356.15
	264	250.59	259.76	265.59	275.94	293.11	292.80	298.44	315.44	330.31	334.41	346.21

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 8 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
15	139	209.58	218.93	224.81	231.30	239.81	249.86	255.06	259.44	270.02	279.21	
	150	205.21	215.27	224.48	232.67	242.22	252.50	260.82	267.24	277.59	285.95	
	157	205.28	213.95	223.19	233.39	239.23	244.93	257.39	266.75	272.86	278.86	
	168	217.79	227.96	238.29	247.37	252.83	261.92	267.33	277.93	286.33	298.98	
	175	216.62	226.11	234.20	245.19	252.60	261.93	270.51	284.14	288.39	300.78	
	185	214.90	228.34	237.48	245.41	251.13	259.09	271.93	277.77	281.49	290.69	
	196	226.31	230.14	242.23	251.64	261.63	269.32	280.14	290.55	299.05	306.34	
	203	224.84	234.03	242.94	251.52	263.90	272.07	279.01	289.77	297.04	309.44	
	214	207.00	215.30	224.20	229.90	243.13	247.02	253.12	261.62	272.33	278.69	
	221	233.71	240.11	254.04	259.73	266.60	279.09	286.17	291.33	298.89	314.24	
	232	214.10	221.18	231.79	238.64	247.50	254.25	260.17	266.23	279.04	287.66	293.29
	239	232.18	241.03	252.04	261.97	274.10	287.58	295.43	307.78	314.81	325.65	337.38
	250	223.27	232.27	243.83	255.76	260.85	264.50	277.29	283.35	288.22	297.66	309.01
	257	256.66	267.40	279.35	291.09	299.61	311.76	319.43	328.84	339.67	349.61	354.74
	267	237.00	250.75	259.36	270.54	275.26	286.49	295.37	307.79	316.63	329.86	337.61
16	140	199.23	204.41	213.27	222.81	230.19	234.48	243.92	249.06	257.48	268.01	
	149	173.33	178.19	185.12	192.57	200.89	204.58	215.32	221.73	228.29	238.23	
	158	198.20	205.24	212.86	220.49	227.98	235.51	243.62	249.63	256.43	265.15	
	167	177.68	184.94	193.81	198.37	204.56	209.08	214.11	220.78	227.06	231.00	
	176	227.91	234.49	242.66	253.06	258.80	267.32	277.59	283.53	294.68	308.27	
	186	210.67	215.88	226.83	234.44	241.69	250.12	264.55	271.05	278.49	284.38	
	195	208.49	215.37	221.11	224.10	230.90	239.14	247.12	249.51	259.52	258.30	
	204	184.38	191.41	197.73	205.50	212.72	221.93	225.24	232.45	238.85	245.31	
	213	204.68	212.28	219.12	229.28	233.68	244.37	251.24	261.08	268.66	281.38	
	222	209.24	214.36	222.80	229.07	234.56	245.29	251.23	255.19	263.39	266.02	
	231	187.50	196.13	204.85	207.87	217.84	222.70	227.94	237.68	242.61	248.70	255.34
	240	223.14	228.40	243.30	246.64	258.82	267.32	273.19	279.58	295.31	306.34	318.45
	249	212.28	218.77	225.14	236.60	240.69	250.99	261.08	269.13	275.24	281.58	291.20
	258	233.59	244.77	253.23	258.07	263.10	272.96	281.29	287.60	300.73	306.15	311.40
	266	230.69	240.97	250.23	257.82	266.21	275.35	285.11	292.43	301.07	303.89	316.26

(continued)

Table A-4. Individual F_1 Male Post Wean Body Weights (g) for Postnatal Days 43 Through 53 (page 9 of 10)

		Postnatal Day										
Group[a]	Animal ID	43	44	45	46	47	48	49	50	51	52	53[b]
17	143	211.92	216.86	227.30	233.77	243.15	243.79	251.67	261.91	265.16	280.29	
	146	223.20	232.47	246.28	254.07	262.35	272.04	277.76	286.90	296.97	298.52	
	161	232.09	239.42	245.07	251.31	252.50	271.94	278.82	283.82	302.21	309.19	
	164	254.60	268.68	278.15	290.52	297.86	303.38	307.86	318.12	331.55	341.20	
	179	253.39	257.62	265.12	276.56	283.38	288.95	300.28	305.76	311.89	326.26	
	189	229.98	239.94	248.28	258.20	264.78	271.73	280.36	288.59	299.23	304.01	
	192	259.81	271.74	280.58	290.78	300.31	303.83	312.82	328.42	337.54	346.92	
	207	227.44	237.05	245.90	254.05	258.82	262.39	277.67	287.78	295.67	305.50	
	210	211.42	218.53	225.40	235.41	242.26	247.04	256.75	265.08	274.32	380.99	
	225	252.73	262.46	269.74	283.59	294.06	301.14	311.77	323.33	329.78	342.80	
	228	234.97	243.04	252.44	255.73	267.68	274.68	284.88	293.06	301.39	314.02	323.93
	243	269.82	284.95	287.80	298.81	318.89	325.14	338.28	347.78	360.08	377.65	390.26
	246	218.41	224.02	231.33	240.69	245.28	248.43	259.34	266.22	273.75	278.24	282.92
	261	228.90	230.40	247.52	254.56	262.49	270.65	282.04	290.62	296.67	305.64	311.10
	263	232.78	240.39	249.37	253.57	262.44	271.20	276.43	287.72	294.15	301.59	311.68
18	144	192.43	201.10	210.14	217.61	227.26	235.67	237.10	248.28	255.39	264.57	
	145	222.50	229.44	236.25	247.48	250.69	259.61	265.29	274.50	282.05	286.16	
	162	206.98	215.58	227.81	236.16	245.17	253.30	258.19	267.77	277.28	283.46	
	163	233.20	243.33	253.89	259.11	272.31	280.66	287.20	296.37	306.06	315.99	
	180	215.19	223.81	230.16	241.50	247.19	254.24	259.82	272.98	276.10	287.01	
	181	198.20	207.12	213.77	224.82	232.43	235.31	239.88	247.80	254.09	264.81	
	190	212.42	220.27	226.58	235.09	245.53	253.99	261.90	270.35	276.53	287.20	
	191	211.11	218.26	223.15	231.38	240.17	245.64	257.25	266.29	272.50	278.76	
	208	221.59	225.47	232.82	239.65	247.49	255.48	261.24	271.98	282.20	285.79	
	209	247.67	252.80	262.68	271.98	280.46	286.19	298.72	308.04	317.30	323.80	
	226	256.85	266.31	279.51	289.99	294.07	306.26	319.17	326.19	337.11	348.78	
	227	244.16	251.52	258.93	267.66	275.88	287.17	294.10	300.41	312.28	320.25	
	244	252.83	258.56	270.60	279.00	293.30	300.18	312.34	321.64	334.68	340.85	354.34
	245	238.94	250.79	256.76	265.02	277.83	283.01	293.57	302.77	316.40	322.93	332.25
	262	218.22	226.88	236.11	243.82	248.04	259.02	272.39	275.50	285.12	296.11	301.69

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.

[b]Includes only those animals scheduled for necropsy on postnatal day 53.

[c]Male was removed from the study because his correct postnatal day 0 could not be confirmed.

[d]Male was removed from the study because it was not dosed on the correct postnatal days.

[e]Male was found dead on postnatal day 37 after dosing (misdirected dose).

[f]Male was euthanized on postnatal day 29 after dosing due to a leg injury.

[g]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).

[h]Male was found dead on postnatal day 50 prior to dosing.

[i]Male was found dead on postnatal day 37 prior to dosing (misdirected dose).

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 1 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
1	1	6.4	7.7	8.1	9.7	10.8	12.2	20.6	6.1	13.8	16.0
	15	.[b]	13.5	11.1	12.2	9.2	15.9	11.8	13.0	12.2	10.4
	32	6.6	8.7	9.6	10.5	13.1	13.9	14.2	14.8	15.6	15.3
	33	7.0	10.1	10.8	10.9	11.3	13.7	14.7	12.9	15.1	14.7
	50	6.3	9.5	9.2	9.7	10.9	11.1	11.9	12.1	14.5	15.9
	51	7.6	7.3	8.5	10.3	9.7	11.4	10.8	11.8	12.5	15.0
	68	8.2	11.5	11.8	11.9	12.7	15.3	15.4	15.2	15.3	19.2
	69	.[c]									
	86	.[c]									
	87	10.1	10.5	11.6	13.7	12.9	15.1	15.2	16.6	18.5	18.7
	104	9.4	10.7	10.9	12.6	12.0	14.5	14.6	15.9	18.3	19.8
	105	8.0	9.2	12.0	12.5	12.1	14.6	12.8	15.1	15.1	15.3
	122	10.6	11.0	13.9	12.5	14.8	14.8	20.5	11.7	16.3	17.4
	123	7.5	9.9	10.9	11.0	12.6	10.8	13.4	12.1	14.9	15.6
	135	.[c]									
2	4	7.1	10.4	5.3	6.9	7.1	10.0	8.8	11.1	11.5	12.2
	18	.[d]									
	29	12.8	.[b]	8.1	9.9	11.2	11.6	12.5	14.0	13.9	15.9
	36	7.2	8.8	8.2	11.7	11.5	12.8	13.8	14.3	14.7	16.4
	47	15.4	7.7	9.2	9.4	11.9	11.5	12.2	14.1	13.0	15.1
	54	11.9	6.3	6.9	9.4	10.2	9.8	11.0	13.0	11.3	18.9
	65	15.2	4.4	7.5	10.4	11.2	12.7	13.3	14.6	14.4	14.3
	72	19.3	1.0	7.6	9.2	11.5	12.8	15.8	14.4	15.2	.[e]
	83	18.3	3.8	7.6	10.2	11.8	11.6	13.0	13.5	14.1	14.1
	90	9.4	6.8	.[b]	.[e]	14.8	14.1	13.3	14.4	16.2	10.5
	101	10.7	7.5	7.7	10.8	10.2	11.6	12.3	14.6	15.4	14.0
	108	7.8	9.1	7.5	14.9	7.1	11.1	13.5	13.1	15.8	.[e]
	119	.[c]									
	126	14.0	4.7	7.7	13.6	9.7	10.4	16.3	10.6	14.2	16.9
	133	8.9	8.8	9.3	11.9	11.7	13.6	13.6	15.5	15.1	17.2

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 2 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
3	5	15.0	0.1	7.6	5.4	7.4	6.9	9.8	10.4	10.8	11.3
	13	9.4	8.5	3.0	8.2	7.9	8.4	10.0	11.3	10.5	12.4
	19	12.0	6.3	5.2	7.5	7.7	9.4	10.2	14.0	12.1	15.6
	28	13.7	3.0	5.4	11.2	6.5	11.3	12.5	14.9	13.4	16.0
	37	10.2	8.6	7.4	7.6	8.1	11.2	11.8	14.6	12.8	15.9
	46	12.4	4.1	8.3	10.1	10.3	10.9	11.3	12.7	13.8	14.4
	55	.[c]									
	64	8.1	9.6	6.7	9.8	11.9	9.5	12.7	16.5	15.3	15.2
	73	11.6	7.7	5.7	9.5	11.2	13.0	12.4	14.3	14.7	15.2
	82	10.2	10.7	4.4	7.5	9.4	9.8	11.7	15.9	13.2	15.8
	91	10.9	10.6	7.6	8.6	8.8	10.6	11.9	13.3	14.0	15.3
	100	9.9	8.3	6.3	7.8	10.4	10.9	11.9	13.7	12.2	14.8
	109	9.9	9.8	6.8	.[e]	.[b]	6.1	10.2	13.7	14.0	14.7
	118	.[c]									
	127	.[c]									
4	6	13.3	0.4	8.2	9.0	10.3	9.6	9.1	10.2	11.6	11.6
	12	6.2	12.9	.[e]	9.7	10.9	11.0	11.5	11.6	12.8	13.7
	20	6.6	7.3	9.4	11.7	.[e]	12.9	16.2	13.1	.[f]	
	27	9.6	9.5	10.2	13.1	13.5	13.9	15.4	16.0	15.4	16.7
	38	8.7	9.3	10.3	12.2	11.9	12.6	14.2	14.8	14.5	14.8
	45	10.5	5.1	10.7	10.9	12.7	11.7	12.6	15.1	13.0	12.1
	56	12.0	8.6	12.3	14.1	13.1	15.2	15.1	17.2	16.4	16.6
	63	11.7	5.5	10.3	12.3	12.2	12.2	14.2	15.3	14.4	17.2
	74	.[c]									
	81	12.6	3.8	11.1	12.6	9.0	11.4	12.7	14.3	12.1	17.1
	92	9.8	8.6	10.5	11.8	11.0	12.8	13.3	14.6	14.1	15.7
	99	8.9	9.6	11.3	13.1	12.6	12.4	14.3	15.6	15.6	20.6
	110	8.8	8.7	10.5	12.2	11.9	13.3	11.9	14.9	13.2	15.6
	117	12.9	5.3	10.7	12.3	11.8	13.0	12.9	16.9	15.0	12.5
	128	12.3	5.8	11.1	12.9	12.0	14.8	13.0	15.5	16.7	18.0

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 3 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
5	7	5.2	9.2	6.8	7.8	12.5	9.6	9.9	9.6	13.9	11.0
	21	6.8	10.0	11.2	11.8	12.1	12.3	.[g]	16.0	16.0	17.6
	26	8.1	7.3	9.6	12.2	12.4	12.1	14.1	17.4	16.3	17.3
	39	6.8	7.4	9.4	11.6	10.3	12.3	13.9	14.6	15.6	16.3
	44	8.4	8.5	9.8	10.8	10.9	12.2	13.0	15.0	14.3	14.2
	57	12.5	4.3	9.2	11.0	12.5	12.8	13.8	15.4	13.9	16.7
	62	10.2	5.4	7.8	9.7	9.3	11.3	11.1	13.7	12.0	14.6
	75	9.1	8.5	9.5	10.1	11.3	9.8	12.3	14.2	13.2	14.5
	80	8.5	7.7	8.9	10.6	10.7	10.9	12.3	14.7	13.1	15.3
	93	16.7	1.9	7.9	11.5	11.6	10.1	12.5	16.1	14.0	16.8
	98	9.0	8.4	10.1	12.6	12.5	12.5	14.5	16.0	13.6	17.6
	111	11.1	7.4	8.7	11.7	12.8	12.8	12.2	16.0	16.0	17.5
	116	10.5	10.3	11.7	13.6	15.1	13.7	16.1	17.5	16.4	18.9
	129	10.6	10.2	11.2	13.4	14.0	14.5	15.0	17.8	17.1	17.5
	132	9.3	8.7	10.1	11.3	13.8	12.1	16.1	17.1	14.1	17.8
6	8	5.6	9.2	8.5	8.7	9.9	11.1	11.2	11.6	13.6	12.2
	11	5.1	10.1	7.2	9.8	10.2	10.8	11.1	11.8	12.8	11.5
	22	9.1	9.5	8.0	13.8	13.3	14.1	13.0	15.1	15.9	17.5
	25	10.4	8.6	11.1	12.3	13.3	11.7	13.2	15.4	13.1	17.0
	40	8.4	8.8	11.2	11.1	13.3	12.9	12.7	15.1	14.4	16.2
	43	8.5	7.4	10.0	10.7	11.4	11.3	11.9	12.2	14.4	13.6
	58	8.8	7.2	9.3	10.6	11.3	11.2	11.1	13.3	12.8	15.3
	61	9.9	9.9	11.6	13.2	12.5	15.2	13.6	16.9	17.4	17.6
	76	10.7	2.4	9.7	10.6	11.1	9.9	12.2	15.0	12.2	16.1
	79	.[c]									
	94	10.6	9.4	10.9	13.3	13.9	13.4	13.4	17.0	13.8	18.4
	97	12.7	7.5	10.6	12.5	14.1	12.6	13.0	16.2	18.5	17.8
	112	11.4	9.3	11.6	13.9	12.5	13.4	13.4	16.0	14.6	18.8
	115	.[c]									
	130	10.3	10.4	11.8	14.3	15.1	15.7	.[e]	20.4	17.5	19.9

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 4 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
7	9	5.9	9.6	7.6	10.6	11.8	12.5	12.4	13.2	15.2	14.2
	10	5.0	9.1	9.3	8.4	13.2	10.5	12.4	12.1	15.7	13.9
	23	12.5	.[e]	9.5	12.9	13.8	10.6	17.1	14.0	11.0	19.9
	24	.[c]									
	41	8.5	8.3	10.0	11.3	13.0	12.5	13.4	15.9	18.6	12.9
	42	12.4	5.8	10.8	12.8	13.1	11.3	13.1	16.3	13.4	18.7
	59	7.8	8.4	7.5	12.3	11.3	12.7	14.0	15.9	15.3	16.4
	60	7.9	7.9	9.0	11.8	11.5	10.8	12.4	15.6	13.1	14.4
	77	8.8	9.9	9.8	13.5	13.2	13.5	14.8	15.8	14.9	15.2
	78	9.6	7.9	11.3	13.6	13.7	13.0	14.6	15.7	20.2	22.4
	95	7.7	8.5	9.8	12.5	12.6	11.6	13.4	13.6	15.2	20.3
	96	10.1	8.7	10.0	12.9	13.6	12.6	13.2	16.3	15.9	17.9
	113	9.4	9.0	10.1	12.9	14.4	13.7	14.5	16.6	15.3	20.7
	114	.[c]									
	131	.[c]									
8	2	10.4	5.4	6.0	14.2	6.0	11.3	10.1	12.1	11.3	11.4
	16	7.2	9.4	11.7	10.5	12.9	14.3	14.1	15.4	16.7	16.8
	31	9.2	8.6	11.6	11.2	12.7	14.5	13.6	15.5	15.4	12.0
	34	6.9	9.6	10.6	10.4	11.8	11.2	14.4	12.8	15.3	15.2
	49	7.9	8.9	10.7	11.2	11.8	12.7	12.2	14.5	15.0	14.9
	52	7.9	9.2	11.7	12.8	13.2	15.2	15.9	17.2	18.9	20.3
	67	11.6	7.4	10.6	11.6	12.7	12.9	14.1	13.6	14.4	16.1
	70	8.4	10.1	14.6	11.9	12.3	14.8	13.6	14.6	15.8	15.3
	85	9.7	10.2	10.2	12.4	12.7	13.7	13.5	15.7	16.0	14.7
	88	10.6	9.6	11.9	11.2	.[e]	14.9	.[e]	14.9	.[e]	20.5
	103	9.2	9.9	12.0	12.5	14.0	14.8	14.7	14.9	14.7	14.4
	106	9.2	9.0	10.1	11.9	12.5	14.4	13.4	12.9	15.4	16.1
	121	9.6	9.7	10.5	11.8	12.5	13.7	14.2	13.9	15.7	16.3
	124	8.4	10.2	11.3	11.6	13.0	12.9	13.4	14.0	16.0	15.4
	134	9.4	9.6	11.5	12.2	13.6	13.8	13.9	15.2	15.0	15.2

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 5 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
9	3	16.5	0.7	7.0	10.2	9.8	12.0	11.2	11.1	12.5	12.1
	14	5.7	11.6	5.7	8.9	10.3	10.6	10.9	11.5	11.9	13.4
	17	.[c]									
	30	.[c]									
	35	10.7	9.0	10.6	11.3	12.3	12.6	13.5	14.1	15.2	15.1
	48	10.0	9.7	12.2	12.1	12.8	14.3	15.6	13.7	16.1	16.8
	53	9.2	5.2	10.0	11.9	13.0	13.7	14.8	13.5	14.6	17.4
	66	13.1	5.7	10.4	12.8	13.4	13.4	14.0	16.1	16.6	15.5
	71	10.8	12.7	7.9	13.3	14.2	13.5	14.7	16.2	16.5	16.2
	84	10.5	8.7	10.8	12.5	13.4	14.1	13.3	15.8	15.8	16.0
	89	14.3	3.6	10.9	12.6	17.3	9.4	14.6	15.2	13.9	14.5
	102	14.1	4.2	16.7	.[e]	12.8	14.3	15.4	15.4	16.9	17.3
	107	20.8	.[b]	8.8	12.1	14.3	14.1	14.6	16.0	16.8	17.2
	120	13.4	6.6	9.5	13.6	14.4	15.5	15.8	15.0	16.9	18.4
	125	7.6	11.3	11.8	11.7	14.7	14.5	14.9	15.7	16.8	16.2
10	136	5.3	7.6	.[e]	.[e]	9.3	10.7	10.9	12.2	10.9	12.1
	153	6.5	10.0	9.7	10.9	12.1	12.4	12.5	15.3	12.5	15.3
	154	7.3	9.1	10.3	10.7	12.5	10.8	13.8	13.9	14.4	14.9
	171	6.5	9.8	9.4	9.8	11.1	12.1	11.7	14.9	12.6	14.3
	172	7.2	8.6	10.3	12.1	13.2	12.2	18.1	15.9	13.8	15.7
	182	5.9	12.6	10.4	13.2	12.4	11.5	19.8	14.5	17.2	18.2
	199	3.4	9.9	10.7	11.3	10.3	13.5	9.3	14.3	15.9	13.9
	200	4.9	10.0	11.4	12.9	13.1	13.5	17.6	15.6	14.9	14.4
	217	4.9	11.4	10.0	9.9	10.4	13.1	14.2	12.3	14.1	.[h]
	218	3.3	10.6	.[e]	16.0	11.7	13.6	14.6	14.2	13.2	15.5
	235	3.2	10.7	10.5	12.8	13.4	15.2	17.4	15.5	17.0	17.0
	236	6.6	9.8	9.4	12.2	11.8	13.0	16.9	12.5	15.2	18.3
	253	6.6	10.0	9.9	11.7	11.0	13.5	15.6	12.5	13.1	14.6
	254	7.4	10.6	10.9	13.1	11.4	13.6	15.8	14.1	14.6	17.8
	270	6.8	11.2	11.1	12.5	12.7	13.9	16.8	14.5	16.8	16.5

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 6 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
11	137	6.0	8.1	8.7	10.8	13.1	11.5	13.2	14.6	12.6	14.4
	152	6.4	9.0	10.0	12.1	12.5	12.2	15.1	17.0	12.9	16.8
	155	6.9	8.8	10.6	11.0	13.0	13.9	14.9	16.9	14.4	16.5
	170	8.1	8.3	11.1	11.2	11.8	12.5	12.6	15.9	14.6	15.5
	173	8.4	9.5	11.2	13.6	13.3	14.9	16.1	18.0	18.3	16.8
	183	7.1	9.6	9.9	11.1	11.4	12.4	13.8	11.9	12.3	15.1
	198	7.4	10.9	11.9	13.1	13.6	14.0	17.5	16.0	16.1	18.5
	201	6.5	9.3	10.2	11.2	11.2	13.2	15.3	13.0	13.2	15.8
	216	3.3	10.3	10.8	12.2	13.2	12.9	17.7	12.8	15.4	15.7
	219	2.9	10.0	10.7	11.9	12.3	13.9	16.6	11.5	15.3	16.0
	234	3.1	8.2	11.7	16.0	13.2	8.3	15.2	11.3	13.8	16.5
	237	7.0	11.4	11.3	12.5	12.8	14.4	17.3	14.9	15.8	17.1
	252	9.7	12.4	12.2	13.3	17.0	12.1	16.0	14.6	17.1	15.5
	255	7.4	10.8	10.1	12.3	12.0	13.4	15.8	13.4	14.8	16.6
	269	6.3	10.5	10.9	13.2	14.0	14.3	16.7	14.2	16.7	17.9
12	138	6.1	8.1	9.5	10.3	9.9	12.2	12.9	13.7	10.8	11.8
	151	7.8	8.7	10.5	11.7	11.8	12.0	13.6	13.9	10.9	11.7
	156	5.9	7.9	9.8	10.5	10.9	12.0	12.5	14.2	10.2	13.6
	169	7.6	8.5	10.6	10.5	10.1	15.0	14.3	17.1	13.8	14.0
	174	8.6	10.8	11.8	13.4	13.1	14.2	15.6	16.2	15.2	14.5
	184	7.0	9.9	10.1	11.6	12.9	12.9	15.5	12.9	13.0	13.4
	197	6.2	9.3	9.8	10.1	11.2	11.4	14.0	12.3	12.4	12.8
	202	6.0	9.5	9.6	10.9	11.8	12.8	15.1	12.6	12.6	14.7
	215	3.9	10.7	11.1	11.9	12.1	14.5	15.7	14.0	14.3	17.5
	220	7.4	10.9	10.0	11.1	12.6	12.7	16.2	12.5	18.7	12.6
	233	6.5	11.0	11.0	11.7	12.7	14.5	15.9	12.5	14.8	15.2
	238	10.0	12.2	11.5	13.5	15.2	14.9	19.3	16.0	14.2	17.7
	251	7.6	9.8	9.8	12.2	11.6	13.5	14.2	12.9	13.5	15.3
	256	6.9	11.8	10.1	10.6	12.2	12.6	16.7	13.1	13.5	14.9
	268	8.3	10.8	9.9	12.5	12.9	13.5	15.0	12.3	14.2	.[e]

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 7 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
13	141	11.8	4.7	11.0	11.1	11.7	11.5	12.5	14.8	11.9	14.8
	148	16.5	1.1	10.8	10.8	11.0	12.6	14.2	16.3	14.4	16.3
	159	10.4	6.4	11.1	10.6	10.3	10.8	12.1	15.7	13.0	13.0
	166	12.8	8.3	12.2	12.3	11.2	13.3	14.3	16.9	14.2	15.9
	177	11.1	10.0	11.8	13.3	12.2	13.7	15.0	17.3	14.9	17.2
	187	6.0	10.9	10.1	11.4	12.1	13.5	16.1	13.4	14.3	15.9
	194	5.6	9.1	9.6	10.7	11.4	13.6	11.0	14.6	12.7	12.9
	205	8.5	11.9	11.4	12.7	13.0	13.7	15.5	12.9	16.2	16.3
	212	7.6	10.4	13.1	10.5	11.4	14.5	15.8	14.9	18.0	14.7
	223	8.1	11.3	10.8	13.1	12.1	15.1	17.1	13.9	16.3	17.9
	230	8.2	9.9	10.0	12.1	11.8	13.2	19.0	8.6	14.4	14.9
	241	7.4	12.3	12.9	13.2	13.0	17.1	18.3	15.9	17.7	17.7
	248	.[e]	.[b]	11.0	12.4	10.9	14.1	15.8	14.6	13.7	17.4
	259	7.4	10.7	10.4	12.4	13.1	13.4	16.8	14.7	16.5	18.3
	265	8.4	12.8	12.1	14.2	13.7	17.4	19.9	17.2	17.2	18.5
14	142	7.0	6.1	9.1	10.8	10.4	10.8	11.5	14.0	11.4	13.4
	147	8.8	7.5	10.7	11.4	10.5	12.3	13.8	16.7	12.3	15.4
	160	6.7	9.9	10.0	10.7	11.6	10.5	14.2	15.8	12.3	14.1
	165	12.3	7.6	10.2	11.3	11.4	11.6	13.7	13.8	12.6	12.5
	178	11.1	10.9	10.9	12.5	12.5	12.3	14.5	14.7	14.3	16.4
	188	6.6	12.2	9.7	8.7	11.1	12.0	15.3	12.9	14.1	16.3
	193	6.2	11.0	10.8	10.9	11.5	12.3	14.7	.[e]	4.0	14.0
	206	6.1	11.3	12.8	.[e]	11.6	12.2	16.3	13.4	15.1	16.6
	211	6.0	11.0	10.1	12.5	13.3	7.6	17.0	11.2	14.5	13.7
	224	7.3	10.4	11.1	11.2	11.7	12.8	16.6	12.8	15.7	16.1
	229	8.9	11.1	12.1	11.9	12.5	15.2	17.6	15.2	16.4	.[e]
	242	7.2	11.8	10.8	11.9	12.0	13.7	16.6	13.5	16.2	17.0
	247	9.0	11.9	11.1	11.9	10.9	15.0	17.0	14.4	15.8	17.9
	260	8.0	10.8	11.3	11.2	12.7	14.0	16.9	15.7	16.2	19.3
	264	9.0	12.9	12.1	13.3	15.2	16.6	19.5	15.6	18.6	19.9

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 8 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
15	139	6.2	9.2	9.3	9.7	10.4	10.6	12.8	13.1	11.9	13.8
	150	7.0	9.3	10.4	9.1	10.2	10.8	11.0	13.9	12.8	13.6
	157	9.6	7.2	9.6	9.6	9.0	11.1	10.5	12.9	11.7	12.5
	168	6.1	10.8	9.0	9.8	10.4	12.7	13.3	14.2	13.6	13.3
	175	7.3	9.0	10.8	10.6	11.8	11.1	12.6	14.9	12.3	13.7
	185	6.2	10.6	9.2	11.5	11.8	11.5	14.7	12.0	13.2	18.1
	196	11.4	12.6	9.3	10.4	12.6	13.1	14.7	12.7	15.0	15.7
	203	5.8	9.9	9.4	11.0	12.1	13.0	14.6	13.0	13.7	15.4
	214	3.5	9.7	9.3	8.3	8.3	9.8	11.0	10.8	10.7	12.8
	221	6.9	10.0	8.7	9.3	10.6	11.2	14.3	10.6	12.8	13.4
	232	4.1	8.1	9.0	9.2	8.8	11.4	13.4	10.7	12.6	13.2
	239	6.7	11.9	8.3	12.2	12.2	12.3	16.5	14.4	14.7	13.7
	250	6.7	11.4	10.4	11.2	11.3	11.5	12.8	12.1	13.2	13.4
	257	9.7	12.2	11.1	12.6	11.4	14.0	16.5	13.5	15.1	17.0
	267	7.6	10.2	10.0	9.6	10.2	11.9	13.6	12.5	13.0	15.7
16	140	15.2	4.8	7.2	9.7	11.3	12.5	11.1	13.8	14.5	13.5
	149	10.6	4.4	9.0	7.8	8.7	9.5	11.1	11.2	13.9	8.9
	158	7.1	10.3	9.6	10.3	9.6	10.4	12.3	13.5	11.8	13.7
	167	9.1	7.8	5.0	6.7	7.0	6.4	10.0	10.0	10.4	9.0
	176	7.9	8.2	11.0	10.7	10.8	10.3	12.4	15.0	11.6	12.8
	186	8.5	10.8	9.3	11.8	10.5	13.1	15.3	12.4	14.6	14.9
	195	6.2	11.2	10.0	12.3	9.6	12.4	14.3	13.1	13.8	14.7
	204	6.9	9.4	9.1	9.6	9.7	10.7	14.6	10.9	11.3	12.6
	213	6.8	10.9	7.8	8.8	8.8	9.6	12.3	10.4	9.5	13.0
	222	8.2	8.7	9.5	9.8	10.0	11.6	14.4	11.3	12.2	14.2
	231	7.0	9.8	6.8	7.7	9.0	9.8	11.1	7.1	10.1	12.7
	240	6.1	9.2	9.5	10.5	10.7	11.2	15.2	12.7	13.3	13.9
	249	12.3	9.6	8.2	10.2	8.9	10.8	13.5	9.5	11.6	12.6
	258	8.2	11.0	10.5	12.0	10.6	13.5	16.3	13.7	15.2	17.4
	266	7.0	12.3	12.1	10.7	10.6	12.4	14.9	12.9	15.4	14.1

(continued)

Table A-5. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 21 Through 31 (page 9 of 10)

Group[a]	Animal ID	Postnatal Days									
		21-22	22-23	23-24	24-25	25-26	26-27	27-28	28-29	29-30	30-31
17	143	10.1	4.1	7.3	10.9	10.9	11.9	12.2	15.3	12.9	14.7
	146	9.6	4.6	11.7	12.1	12.5	12.8	13.5	14.9	12.9	13.8
	161	8.0	9.4	11.8	11.9	11.1	12.3	15.3	14.2	14.2	15.1
	164	9.7	7.1	10.6	13.0	12.3	12.3	14.4	16.4	15.5	15.9
	179	10.0	11.9	14.4	13.3	15.4	14.4	16.3	17.7	15.9	17.7
	189	9.2	10.5	11.5	11.9	12.3	13.5	15.4	12.4	14.5	13.9
	192	6.3	10.5	13.2	13.7	12.6	15.1	17.4	15.2	16.9	20.2
	207	8.4	10.9	12.7	12.2	12.2	14.0	16.1	13.4	16.3	15.5
	210	8.2	11.4	11.2	10.8	11.1	12.8	13.7	11.5	14.0	14.5
	225	7.4	12.1	12.3	13.0	13.8	14.7	16.2	14.2	16.5	15.4
	228	7.6	13.7	12.5	12.3	12.9	12.9	14.0	15.3	14.5	14.2
	243	8.3	11.6	12.7	13.1	14.1	15.6	19.4	15.4	16.3	17.6
	246	8.3	12.3	12.7	12.8	13.1	14.1	15.8	13.1	15.1	15.4
	261	6.7	10.2	11.7	12.7	13.4	12.9	14.5	13.3	15.1	15.3
	263	6.2	11.5	12.8	12.8	13.5	13.6	15.2	15.0	15.7	16.9
18	144	6.1	8.7	10.8	10.5	12.4	12.5	14.3	16.6	12.4	16.3
	145	11.9	3.7	10.4	11.3	10.9	12.3	14.1	14.7	14.9	15.6
	162	6.9	8.7	10.4	11.9	11.9	13.2	13.8	15.8	13.3	15.1
	163	8.0	7.6	7.7	8.9	10.9	11.9	15.4	15.1	14.6	15.3
	180	7.9	8.3	12.1	11.5	12.5	14.3	14.1	16.8	13.6	15.2
	181	9.3	4.7	10.4	11.0	12.0	13.1	12.8	14.9	12.6	13.8
	190	7.7	10.9	10.7	12.4	13.0	13.4	15.4	13.0	15.4	14.6
	191	7.1	11.4	11.1	12.2	13.4	13.1	15.7	13.4	14.7	17.4
	208	6.5	11.7	11.6	12.5	13.0	16.0	16.8	14.4	17.6	18.0
	209	7.8	12.1	11.3	13.1	13.7	15.2	16.8	14.4	15.5	17.7
	226	7.2	13.3	12.5	13.4	13.7	15.2	18.6	16.6	19.2	18.5
	227	9.9	7.8	9.7	12.5	13.2	13.5	17.5	10.3	16.1	16.5
	244	4.6	10.5	11.1	11.9	13.7	15.2	17.2	14.7	17.5	17.7
	245	6.0	12.0	11.0	11.1	15.0	14.7	17.3	14.6	14.9	16.4
	262	7.2	10.7	12.1	14.0	14.0	15.8	13.5	14.5	25.3	.[e]

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.
[b]Feed consumption value was excluded because it was unrealistic (i.e. negative).
[c]Male was removed from the study because his correct postnatal day 0 could not be confirmed.
[d]Male was removed from the study because it was not dosed on the correct postnatal days.
[e]Feed consumption value was excluded because it was a statistical outlier.
[f]Male was euthanized on postnatal day 29 after dosing due to a leg injury.
[g]Feed weight inadvertently not recorded.
[h]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 1 of 10)

Group[a]	Animal ID	Postnatal Days										
		31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
1	1	15.3	17.4	16.6	18.0	21.1	24.7	19.4	21.7	24.8	22.1	21.3
	15	16.7	14.9	16.0	19.4	19.3	21.4	16.4	19.4	21.0	22.3	23.3
	32	18.3	17.7	19.9	22.5	23.6	23.7	22.5	24.5	25.8	20.0	22.6
	33	17.5	17.6	16.5	20.8	19.6	22.9	20.8	18.4	22.1	22.3	25.4
	50	17.7	18.1	19.4	20.7	22.3	23.1	23.4	23.8	24.3	22.7	27.9
	51	13.8	14.9	20.6	16.5	19.5	19.4	20.2	20.0	22.3	23.2	22.3
	68	17.8	16.8	19.3	21.1	21.5	19.8	20.7	22.6	20.9	21.8	24.8
	69	.[b]										
	86	.[b]										
	87	22.8	21.0	25.9	24.1	25.4	23.5	24.0	26.3	25.0	36.1	16.9
	104	18.2	20.6	20.9	23.7	24.2	24.5	25.2	23.5	26.8	27.7	.[c]
	105	17.1	17.7	20.2	19.3	22.7	22.0	22.4	23.7	24.4	30.3	24.0
	122	15.6	18.5	18.7	24.5	16.2	21.1	20.2	20.8	23.8	24.9	24.6
	123	18.0	19.2	18.5	18.3	19.1	20.0	19.9	21.7	21.9	21.6	22.2
	135	.[b]										
2	4	13.5	13.9	14.5	15.9	22.8	15.7	16.9	19.8	18.6	21.2	19.9
	18	.[d]										
	29	16.6	17.9	19.2	21.0	24.0	20.8	19.0	22.3	21.8	24.9	23.6
	36	16.6	16.0	18.8	21.0	23.3	19.6	22.1	20.2	24.4	19.7	21.5
	47	17.6	15.7	18.0	21.1	22.8	18.7	18.7	20.5	22.0	22.6	23.5
	54	15.6	16.1	.[c]	23.7	.[c]	19.5	.[e]				
	65	17.7	17.9	19.8	20.9	25.9	19.3	21.4	23.1	23.4	24.7	23.2
	72	14.4	15.4	21.5	20.3	28.9	25.2	21.5	.[c]	17.3	29.1	.[c]
	83	17.3	16.3	19.2	19.1	24.2	19.8	18.4	22.0	23.5	21.0	26.0
	90	7.1	5.1	17.9	21.5	24.1	21.4	17.2	24.2	22.8	23.5	22.7
	101	17.2	15.3	16.6	.[c]	.[f]	18.6	20.0	21.8	19.7	23.0	26.1
	108	.[f]	20.0	16.9	23.4	18.0	24.9	18.4	21.6	22.9	25.5	23.3
	119	.[b]										
	126	17.3	14.3	17.4	23.2	22.4	17.9	19.2	23.3	20.9	22.9	25.4
	133	17.7	18.2	17.9	21.3	24.7	20.8	20.8	21.6	24.0	25.2	22.9

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 2 of 10)

Group[a]	Animal ID	Postnatal Days										
		31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
3	5	12.7	13.1	13.7	14.6	18.9	20.2	15.8	17.5	20.3	18.7	25.8
	13	12.6	12.5	13.1	13.8	18.5	19.3	14.3	15.0	22.8	18.6	21.1
	19	16.2	16.7	19.2	19.3	29.3	18.0	18.5	23.6	25.0	24.2	20.0
	28	18.2	15.5	17.7	18.4	25.2	17.5	19.2	22.1	23.5	24.7	20.7
	37	15.0	.[f]	.[c]	18.9	23.5	16.1	16.0	20.0	20.3	22.3	19.3
	46	14.1	15.5	15.9	21.8	20.4	17.5	18.8	19.6	20.9	21.4	20.5
	55	.[b]										
	64	15.8	14.1	17.1	21.9	24.6	18.0	17.9	24.5	28.2	21.2	22.0
	73	17.8	17.2	16.6	22.4	26.4	19.2	18.0	23.0	23.1	22.6	23.6
	82	23.8	10.8	20.3	18.2	23.0	16.7	20.6	23.4	19.4	22.6	25.0
	91	17.2	16.3	17.8	23.2	28.6	18.1	.[c]	.[f]	25.5	26.8	23.1
	100	16.4	16.2	17.4	20.1	22.3	19.9	20.6	21.0	23.9	21.0	23.7
	109	17.3	17.0	14.5	23.7	21.4	14.1	16.1	19.4	18.9	20.6	18.8
	118	.[b]										
	127	.[b]										
4	6	11.0	13.3	13.1	13.9	15.6	18.7	17.1	16.6	19.7	19.1	22.5
	12	12.2	10.5	21.3	.[c]	21.1	21.4	21.8	17.6	22.5	24.8	23.2
	20	.[g]										
	27	19.3	17.8	20.4	20.4	21.9	22.9	22.8	26.5	23.1	26.8	27.1
	38	18.4	17.2	19.9	21.2	20.2	20.3	22.1	23.8	24.5	26.5	24.5
	45	15.8	15.1	18.5	19.5	20.1	18.0	20.3	22.1	24.2	24.6	23.1
	56	19.0	20.2	23.1	21.1	26.0	25.2	20.9	24.2	27.1	25.6	26.9
	63	17.6	17.1	18.2	20.0	23.6	20.5	21.0	26.0	24.0	26.5	25.1
	74	.[b]										
	81	.[f]	.[c]	17.7	20.8	24.3	25.4	19.8	27.0	27.2	26.2	27.5
	92	16.3	17.0	14.9	19.7	22.3	23.9	19.5	22.2	23.9	24.3	22.4
	99	19.1	17.5	19.4	20.7	26.1	23.3	23.4	25.3	28.4	27.5	24.1
	110	16.6	17.2	15.5	21.4	27.1	21.9	22.4	23.4	25.3	25.7	21.8
	117	6.4	4.6	3.0	20.1	30.8	22.5	23.6	25.6	26.3	27.0	23.4
	128	20.2	17.3	18.7	21.1	24.8	25.0	22.2	26.1	28.0	25.2	25.6

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 3 of 10)

		Postnatal Days										
Group[a]	Animal ID	31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
5	7	13.1	17.6	13.7	19.5	17.2	17.1	16.0	17.9	20.2	22.9	22.7
	21	19.1	19.5	20.3	19.4	26.2	24.2	26.3	28.7	26.3	26.1	25.7
	26	22.7	21.4	21.4	23.0	28.6	22.7	26.3	25.9	28.7	26.6	27.1
	39	18.1	17.8	17.6	18.5	23.5	22.4	22.9	23.0	25.9	27.3	21.0
	44	19.5	17.7	19.2	18.6	24.1	23.4	25.1	21.9	26.6	24.9	23.4
	57	19.2	17.2	18.2	21.8	26.3	24.2	24.3	26.0	24.5	26.0	26.8
	62	17.2	15.4	18.9	21.0	17.7	22.0	19.6	22.9	22.0	23.3	23.4
	75	16.1	17.1	15.9	18.6	23.1	22.5	18.8	25.1	23.1	21.1	25.0
	80	14.6	17.0	16.9	19.3	24.8	20.5	21.6	25.6	23.8	24.4	26.6
	93	18.0	19.0	20.8	19.3	23.3	22.4	21.6	26.5	25.4	24.4	27.3
	98	18.7	19.3	21.0	19.7	25.1	21.4	24.3	26.7	25.8	24.9	25.2
	111	19.7	18.1	21.4	22.5	25.9	25.8	25.9	25.5	26.1	28.7	31.8
	116	20.7	21.0	21.9	24.0	24.6	27.0	26.0	24.5	30.1	24.1	28.4
	129	19.2	20.5	24.4	21.8	27.9	23.1	23.6	27.3	28.6	26.1	30.6
	132	19.6	18.1	20.6	21.3	24.3	23.4	24.3	22.6	26.2	23.9	26.9
6	8	14.4	14.8	16.6	14.9	16.4	18.7	19.0	20.2	19.9	22.9	20.4
	11	14.6	16.0	15.8	15.3	18.1	20.0	19.0	20.9	19.9	23.8	21.5
	22	20.1	17.7	19.2	22.9	26.0	28.6	23.1	26.0	28.4	30.1	28.1
	25	17.6	16.8	16.5	19.1	23.7	21.7	19.2	21.5	22.5	22.5	23.6
	40	17.7	17.0	18.9	22.4	23.5	24.6	22.1	24.8	28.0	23.3	25.7
	43	15.3	14.1	15.0	18.2	21.2	19.4	20.2	16.8	22.2	21.4	21.5
	58	15.9	15.0	16.0	18.3	20.6	20.7	19.9	22.9	22.5	23.2	23.1
	61	19.1	18.5	18.9	19.7	25.1	22.1	20.9	22.7	26.5	21.9	25.8
	76	17.5	16.9	15.1	18.4	26.1	21.6	18.6	25.3	24.3	24.5	26.2
	79	.[b]										
	94	19.0	19.5	18.7	23.3	27.4	25.5	23.3	28.7	30.2	26.5	27.1
	97	22.8	17.6	18.0	14.7	24.7	22.6	20.9	23.5	25.4	22.8	24.4
	112	16.0	17.3	19.7	21.3	25.8	22.3	24.6	27.3	25.7	23.9	.[c]
	115	.[b]										
	130	22.4	21.7	24.9	25.4	31.1	26.0	26.4	30.9	30.8	30.3	31.0

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 4 of 10)

Group[a]	Animal ID	Postnatal Days										
		31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
7	9	15.8	17.0	15.9	17.3	19.8	21.0	20.6	21.8	23.1	24.4	23.8
	10	14.3	17.2	16.2	18.1	19.1	21.0	22.3	21.0	20.7	23.8	26.0
	23	19.5	.[c]	15.1	18.9	20.7	20.2	21.2	23.3	25.0	24.4	26.0
	24	.[b]										
	41	18.4	16.9	17.9	19.3	20.8	22.6	22.0	22.1	24.5	24.6	23.3
	42	17.5	16.1	18.8	19.4	22.0	23.5	21.9	24.5	25.0	23.2	24.9
	59	19.4	17.5	20.9	20.1	24.3	21.4	22.2	23.2	25.8	23.2	25.1
	60	16.7	16.2	18.4	20.1	24.3	22.4	20.7	23.8	22.9	25.8	24.3
	77	18.1	13.8	16.9	18.1	21.0	20.0	18.2	19.3	23.5	23.3	21.5
	78	19.0	19.7	19.0	19.5	22.8	22.6	.[c]	19.5	26.5	19.3	22.7
	95	17.4	17.9	17.9	19.0	20.7	21.8	22.0	23.8	23.4	23.8	22.2
	96	20.9	14.8	20.0	20.6	23.2	24.5	20.9	22.7	25.4	24.6	28.6
	113	17.9	16.7	19.5	20.6	24.3	23.9	24.4	26.7	27.5	28.6	24.1
	114	.[b]										
	131	.[b]										
8	2	13.5	12.9	23.6	15.0	16.1	22.0	15.0	17.8	17.6	20.1	18.5
	16	17.3	17.8	19.9	20.9	22.3	26.0	21.5	22.5	26.3	25.9	25.6
	31	6.9	6.1	8.1	8.5	18.8	20.3	19.4	22.4	21.9	19.9	23.6
	34	16.6	17.7	18.5	19.0	22.5	19.5	22.1	12.9	19.9	24.9	22.4
	49	17.8	19.6	17.2	22.9	20.6	21.3	19.9	21.6	21.5	23.1	26.8
	52	19.2	21.6	27.8	24.5	26.9	26.6	27.3	30.0	27.0	26.7	32.8
	67	17.8	21.7	11.4	21.0	22.6	18.3	19.9	22.5	24.7	20.7	25.0
	70	17.3	22.2	15.0	22.7	23.5	20.8	22.6	22.4	24.6	22.3	25.7
	85	16.7	18.9	22.0	20.6	24.8	23.3	22.6	24.2	25.0	21.8	24.5
	88	.[c]	16.9	.[h]	23.7	18.0	20.6	22.0	22.8	22.1	22.2	26.3
	103	16.0	21.1	14.1	19.3	22.1	20.6	22.3	22.3	22.0	23.2	25.3
	106	16.6	17.4	19.9	20.3	21.9	19.0	21.2	19.3	21.3	23.6	22.1
	121	17.5	18.5	18.8	21.4	23.2	21.9	22.1	21.9	25.4	23.7	26.0
	124	19.1	15.3	20.2	16.1	22.8	20.6	19.8	21.1	19.8	22.1	20.0
	134	18.2	18.3	20.7	23.0	23.7	21.4	23.4	23.3	24.8	.[f]	24.6

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 5 of 10)

		Postnatal Days										
Group[a]	Animal ID	31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
9	3	13.7	14.4	15.6	12.8	17.4	18.6	17.7	16.1	15.5	18.4	18.8
	14	13.4	14.5	12.8	14.3	19.7	20.8	15.9	19.6	20.3	17.8	22.9
	17	.[b]										
	30	.[b]										
	35	17.1	17.9	19.6	23.2	21.0	22.0	26.3	19.4	28.3	22.1	.[c]
	48	14.5	19.1	19.9	20.2	24.1	26.3	18.4	21.6	28.3	23.5	24.4
	53	18.5	18.9	19.3	20.5	23.3	20.5	25.8	17.9	25.4	21.9	25.7
	66	19.5	21.0	20.0	23.6	27.0	19.0	22.1	23.8	26.0	18.6	28.4
	71	18.1	18.6	25.0	38.8	6.6	21.9	21.6	25.2	24.0	22.5	23.9
	84	18.3	17.8	17.8	38.2	7.1	21.7	21.1	21.0	25.5	24.6	23.2
	89	17.5	17.4	17.9	18.4	24.7	19.7	22.9	21.4	22.1	25.0	22.8
	102	20.9	19.8	20.6	17.9	27.9	23.1	20.4	24.7	22.8	25.7	26.0
	107	20.3	19.8	22.3	23.8	24.9	25.0	23.0	24.3	23.9	23.5	26.4
	120	18.3	20.1	23.5	21.9	25.9	26.1	25.3	25.6	27.1	27.6	26.5
	125	16.3	25.3	19.8	31.3	15.9	23.0	25.9	21.5	24.0	29.6	21.7
10	136	13.1	13.7	16.4	14.5	16.5	17.5	17.7	20.5	20.5	18.2	18.4
	153	15.4	16.3	17.8	17.0	18.8	20.8	21.3	20.6	21.5	23.6	24.3
	154	16.4	16.5	18.1	19.0	19.8	22.5	21.9	23.3	24.3	20.6	22.9
	171	15.1	17.3	19.4	23.3	15.6	22.2	22.7	23.8	20.6	24.5	23.9
	172	18.1	16.8	19.7	18.7	20.5	20.8	22.8	20.0	24.5	23.7	24.3
	182	21.4	25.9	17.8	27.0	26.5	22.5	25.1	28.0	26.2	25.2	30.9
	199	18.7	18.6	20.4	10.2	20.3	22.7	20.3	26.0	24.3	24.3	27.2
	200	18.6	19.7	18.1	22.8	21.5	22.5	24.9	19.9	24.7	22.0	24.1
	217	.[i]										
	218	17.0	19.2	17.2	19.6	18.3	22.0	20.2	23.2	20.6	22.4	23.3
	235	20.8	24.0	19.9	21.0	25.1	24.5	26.2	21.8	22.8	24.3	24.9
	236	18.1	17.3	19.2	22.0	20.0	23.9	23.5	23.4	22.7	23.0	24.4
	253	15.9	16.5	16.2	18.8	19.7	20.4	20.3	22.4	21.9	20.7	26.1
	254	17.7	17.8	18.0	19.8	20.4	21.8	20.9	22.9	21.4	22.2	23.1
	270	18.5	19.8	20.1	20.7	23.1	22.1	24.1	22.7	24.3	24.7	22.4

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 6 of 10)

		Postnatal Days										
Group[a]	Animal ID	31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
11	137	16.7	15.2	16.7	20.9	16.8	19.2	19.6	19.1	18.8	20.2	17.1
	152	17.1	17.3	19.4	17.5	25.1	19.7	20.9	23.3	22.4	22.5	21.9
	155	18.3	19.6	20.3	20.1	22.8	20.8	23.9	23.6	22.2	23.3	20.8
	170	18.3	19.5	22.2	.[c]	25.1	22.5	21.6	22.7	23.6	23.0	20.1
	173	20.6	20.1	22.2	22.4	25.1	26.6	25.2	23.8	26.6	27.0	27.6
	183	18.4	15.5	15.5	19.4	18.9	20.9	20.0	22.0	24.1	19.1	21.5
	198	19.4	18.6	18.5	21.1	21.5	24.4	24.0	20.0	23.8	23.7	24.6
	201	16.9	17.9	17.6	21.3	19.6	19.3	27.0	24.3	21.1	23.4	26.5
	216	16.9	18.4	17.5	20.4	20.2	25.9	21.9	23.2	24.9	22.8	26.5
	219	17.0	17.3	18.4	20.6	19.1	21.7	21.2	22.1	22.8	21.6	25.4
	234	15.7	17.5	19.5	19.4	18.3	21.6	19.9	21.5	21.3	21.2	22.3
	237	18.9	21.1	18.1	21.1	21.6	23.1	23.0	22.1	26.5	22.0	24.5
	252	19.3	18.2	20.3	20.4	23.0	26.4	21.6	24.4	25.3	24.4	25.7
	255	18.1	17.0	18.1	19.8	20.4	21.0	21.7	22.4	23.7	20.9	21.9
	269	18.0	19.9	18.8	24.0	21.4	23.2	24.5	24.1	23.7	23.3	24.6
12	138	.[c]	18.1	10.8	24.5	10.9	11.1	11.9	13.7	10.0	8.0	9.8
	151	12.0	11.3	10.9	10.8	11.0	9.8	10.3	9.8	9.7	9.3	9.0
	156	12.9	14.0	12.8	18.7	13.0	12.7	12.0	11.2	12.2	11.5	12.2
	169	16.6	16.7	15.1	15.6	14.0	13.5	15.1	13.2	15.1	13.1	12.6
	174	16.6	11.4	14.5	13.7	15.4	14.5	22.8	4.4	13.5	10.0	12.1
	184	11.4	11.7	10.7	12.8	11.8	11.6	11.9	11.8	11.6	9.9	11.6
	197	13.6	12.9	13.7	13.1	13.2	13.5	13.5	14.2	13.2	12.5	12.8
	202	13.6	12.6	11.3	14.4	12.7	12.8	18.4	6.4	11.4	10.7	12.0
	215	16.1	17.0	14.9	17.8	15.8	17.6	17.2	15.3	16.8	12.3	16.5
	220	14.4	16.1	22.8	9.5	14.9	14.6	15.8	19.0	13.5	12.5	13.8
	233	15.0	15.0	14.5	15.4	15.0	14.0	12.9	19.1	12.4	12.5	14.0
	238	16.3	16.1	14.7	14.7	16.5	13.9	15.5	13.0	15.0	12.5	13.9
	251	14.5	15.2	13.7	14.1	15.1	14.3	23.7	9.6	13.5	12.3	13.5
	256	16.9	16.4	15.4	16.4	15.2	16.1	16.7	14.7	15.2	14.6	15.1
	268	14.5	14.1	13.4	13.5	13.7	14.0	12.6	14.4	12.9	10.6	13.4

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 7 of 10)

		Postnatal Days										
Group[a]	Animal ID	31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
13	141	14.9	16.3	19.2	9.4	18.5	24.5	19.0	14.0	23.1	.[c]	18.8
	148	18.2	19.6	20.0	22.2	21.5	24.6	26.7	25.8	24.0	24.9	25.0
	159	15.0	14.8	16.8	15.7	19.6	18.3	20.1	20.9	18.5	19.5	19.1
	166	17.6	18.8	19.8	19.7	22.0	21.0	32.3	16.6	28.5	25.8	22.1
	177	17.4	20.5	21.8	21.5	24.3	24.2	25.8	25.6	26.5	25.5	24.4
	187	16.3	17.3	18.3	21.8	18.9	22.4	20.8	23.0	25.9	25.3	25.7
	194	14.7	17.1	16.8	17.3	18.5	21.0	20.2	21.9	20.1	24.3	22.7
	205	17.5	19.0	19.6	18.9	22.7	26.5	22.0	23.0	23.0	23.1	26.6
	212	16.6	21.0	17.1	22.5	21.5	24.9	23.2	24.6	21.9	22.8	26.5
	223	19.5	18.9	22.1	21.6	20.3	26.1	22.1	26.7	24.1	23.6	27.4
	230	16.3	18.8	19.1	19.5	20.6	22.4	17.8	21.8	21.6	22.0	22.7
	241	19.8	23.2	21.1	24.8	23.6	28.8	25.4	27.0	25.4	25.3	27.5
	248	17.1	18.3	18.2	20.2	19.3	24.1	21.7	21.5	22.4	24.4	24.4
	259	18.9	19.1	20.9	21.7	22.0	23.9	29.2	20.6	25.5	23.3	26.0
	265	19.7	20.8	19.1	23.8	24.2	27.3	26.0	24.8	25.3	23.6	30.5
14	142	15.0	13.1	15.8	17.5	17.9	19.3	19.7	20.5	20.9	18.8	22.0
	147	14.1	17.1	23.0	17.8	17.7	18.7	22.0	21.0	19.4	19.8	25.2
	160	14.0	15.8	17.1	17.5	20.0	20.1	23.1	23.7	24.2	17.6	24.5
	165	15.5	12.0	16.5	16.9	19.1	16.9	22.4	18.9	20.3	21.3	21.2
	178	17.2	18.3	19.7	20.7	22.4	23.4	24.7	22.0	25.6	23.3	24.8
	188	15.8	16.7	17.5	.[f]	.[c]	22.1	21.3	20.7	21.1	26.7	24.8
	193	15.9	17.5	17.3	21.2	18.5	20.0	21.1	22.0	20.9	23.7	23.4
	206	16.7	20.3	16.7	20.1	19.1	23.2	22.1	22.3	21.5	21.2	24.1
	211	13.9	16.9	14.3	20.2	17.2	21.0	18.9	26.9	17.3	15.5	28.8
	224	20.1	16.4	16.7	22.6	20.8	23.8	21.7	21.7	23.4	20.7	27.4
	229	17.8	22.2	21.8	22.6	21.3	25.9	24.0	24.1	25.6	30.1	28.2
	242	17.1	20.0	19.3	21.9	22.6	.[j]					
	247	20.3	19.1	20.8	23.4	24.1	22.9	24.3	26.5	23.6	.[c]	.[c]
	260	15.8	20.1	18.0	23.0	22.9	25.7	24.7	30.3	23.9	26.3	29.3
	264	16.3	21.5	18.3	23.1	21.2	23.3	24.0	22.3	23.7	29.0	24.6

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 8 of 10)

Group[a]	Animal ID	Postnatal Days 31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
15	139	14.7	15.4	16.2	16.8	19.2	19.2	20.7	19.0	20.3	20.6	21.9
	150	14.8	14.3	15.9	18.4	18.4	19.4	19.9	20.5	26.0	22.1	17.5
	157	13.5	14.0	19.6	17.4	20.0	19.0	21.2	22.4	22.9	23.1	25.3
	168	15.9	17.0	18.0	16.3	20.5	18.8	21.7	19.9	21.1	23.7	23.4
	175	13.9	15.2	16.9	19.4	18.2	20.0	21.0	29.0	19.0	19.6	21.6
	185	14.2	17.5	19.7	19.2	18.1	22.4	20.3	20.9	23.0	21.8	22.0
	196	15.3	22.0	8.0	15.3	17.9	21.0	18.4	22.2	21.5	20.3	25.1
	203	14.8	16.9	20.5	21.0	20.3	20.8	21.5	23.3	23.3	22.6	23.8
	214	14.0	14.7	15.4	18.8	17.3	20.8	18.1	22.9	21.7	22.6	23.8
	221	14.6	17.5	16.3	18.7	19.6	21.7	19.9	21.9	20.6	23.5	22.9
	232	14.6	16.1	21.7	17.5	17.9	18.7	20.1	21.8	22.8	21.1	23.2
	239	17.2	16.3	18.9	18.1	19.2	20.8	21.2	22.0	21.3	24.8	23.0
	250	14.7	16.1	16.2	18.3	17.4	22.4	17.9	21.2	20.3	21.7	22.1
	257	18.7	18.9	21.7	21.4	22.6	25.6	23.3	28.0	26.2	25.8	29.1
	267	17.6	20.5	16.8	20.7	22.5	21.7	20.9	25.2	22.6	23.9	24.9
16	140	13.5	16.4	14.3	17.5	19.0	19.6	20.5	29.7	10.0	21.8	22.7
	149	12.2	13.1	14.4	15.4	15.4	17.0	19.7	38.1	.[f]	20.3	12.6
	158	14.7	14.0	13.7	17.0	19.4	19.6	19.9	25.5	15.1	19.2	21.7
	167	11.6	11.0	14.3	14.9	12.9	14.0	15.8	14.7	21.0	15.8	16.4
	176	15.1	14.0	18.6	19.1	20.0	23.0	21.0	24.1	25.2	22.4	26.9
	186	14.4	17.6	15.2	19.9	19.1	25.8	20.9	19.6	18.6	22.3	21.1
	195	16.1	16.8	16.6	17.1	20.0	19.0	19.9	19.8	17.9	22.4	19.3
	204	11.6	13.9	14.2	17.5	16.9	17.1	18.2	18.0	16.7	17.5	21.3
	213	13.3	14.5	12.9	18.5	16.8	17.7	24.8	12.4	20.5	18.5	20.3
	222	14.0	16.5	14.5	17.8	20.2	21.9	16.5	21.4	20.4	22.4	22.7
	231	11.1	12.9	13.3	15.9	19.0	15.1	26.0	10.8	16.2	17.0	18.7
	240	15.1	16.8	16.3	18.0	21.7	19.3	24.7	20.0	20.1	23.3	31.4
	249	13.0	14.0	16.6	16.5	15.8	18.7	19.7	18.4	18.3	17.5	23.6
	258	16.6	19.2	17.4	21.1	23.5	24.0	29.9	17.3	23.0	19.3	26.9
	266	14.9	16.7	16.7	19.6	25.5	18.1	21.6	22.6	19.8	21.6	25.3

(continued)

Table A-6. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 31 Through 42 (page 9 of 10)

Group[a]	Animal ID	Postnatal Days										
		31-32	32-33	33-34	34-35	35-36	36-37	37-38	38-39	39-40	40-41	41-42
17	143	15.0	11.0	16.6	17.0	20.5	20.1	21.3	23.0	25.3	20.6	19.7
	146	15.7	15.1	16.7	19.3	19.5	20.4	21.9	24.8	27.5	18.5	22.8
	161	18.6	14.6	18.8	18.2	26.1	23.4	.[c]	29.6	14.1	6.8	.[c]
	164	17.1	18.9	19.9	20.8	24.2	23.5	24.1	25.4	26.5	25.7	27.7
	179	18.5	19.9	19.5	21.6	21.3	23.1	23.3	24.7	30.2	21.1	29.2
	189	16.3	18.0	17.1	18.9	20.0	23.1	27.8	16.6	22.4	23.6	27.6
	192	18.9	21.0	21.3	23.5	23.0	25.4	26.6	24.2	26.3	25.4	28.3
	207	17.6	19.3	17.4	19.2	20.7	22.1	25.9	18.8	21.9	23.5	23.2
	210	14.0	16.5	16.6	17.3	18.6	20.2	24.8	16.0	20.4	19.0	27.2
	225	18.6	17.8	17.7	.[c]	12.8	.[c]	23.3	.[f]	25.3	27.4	28.8
	228	17.3	17.6	19.9	21.4	19.8	23.3	23.7	25.1	21.4	23.4	25.8
	243	18.3	20.3	18.5	23.1	23.0	29.8	24.7	32.0	25.6	39.4	30.9
	246	15.5	18.6	15.8	18.4	18.2	20.8	20.0	19.6	20.3	19.7	25.7
	261	17.1	18.5	17.9	20.4	20.5	21.5	22.8	22.6	23.3	23.2	28.5
	263	17.1	18.4	18.4	21.0	20.4	23.5	23.1	22.8	21.6	22.1	23.6
18	144	14.4	15.9	16.9	17.6	20.3	18.4	21.4	14.7	20.6	18.0	23.3
	145	19.0	17.2	17.8	17.2	19.0	20.5	23.7	24.0	24.5	24.3	24.9
	162	15.1	14.7	17.5	18.7	17.7	18.8	20.7	20.3	20.6	20.5	20.6
	163	17.0	18.0	16.5	20.1	20.6	24.1	23.3	26.4	26.8	20.5	26.8
	180	16.1	15.8	16.9	18.7	19.2	18.8	22.2	20.7	22.9	18.3	22.2
	181	14.7	15.2	16.1	19.1	18.4	17.3	19.3	19.1	21.1	20.8	21.4
	190	14.8	25.4	21.7	11.1	18.9	20.8	34.4	23.4	10.4	23.4	25.4
	191	14.0	17.2	15.9	19.4	19.1	20.7	18.2	19.6	20.5	21.4	22.3
	208	15.8	18.0	17.4	20.4	19.0	29.7	10.8	21.3	23.1	21.1	24.3
	209	18.1	19.3	24.6	21.6	22.8	25.0	24.9	26.1	26.8	23.6	29.2
	226	19.6	19.5	21.4	24.3	22.4	25.7	24.2	27.7	28.0	26.2	29.8
	227	16.1	18.2	19.8	21.4	21.8	31.7	16.4	25.1	25.2	24.6	26.9
	244	18.1	19.7	20.1	21.0	23.3	24.7	25.9	25.4	26.8	25.9	26.7
	245	16.3	23.5	18.3	21.6	18.4	20.5	21.2	23.4	26.5	22.6	29.9
	262	14.9	17.1	15.7	17.9	16.4	19.1	21.3	15.7	24.9	21.1	23.7

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.

[b]Male was removed from the study because his correct postnatal day 0 could not be confirmed.

[c]Feed consumption value was excluded because it was a statistical outlier.

[d]Male was removed from the study because it was not dosed on the correct postnatal days.

[e]Male was found dead on postnatal day 37 after dosing (misdirected dose).

[f]Feed consumption value was excluded because it was unrealistic (i.e. negative).

[g]Male was euthanized on postnatal day 29 after dosing due to a leg injury.

[h]Feed consumption value was excluded because the animal had pulled feed into the cage and an accurate feed weight could not be obtained.

[i]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).

[j]Male was found dead on postnatal day 37 prior to dosing (misdirected dose).

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 1 of 10)

		Postnatal Days												
Group[a]	Animal ID	42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
1	1	16.8	33.7	23.8	.[c]	23.0	24.2	21.1	28.1	19.7	22.6		.[d]	
	15	24.4	23.3	22.5	22.3	25.2	22.3	24.5	24.6	26.1	23.1		18.8	
	32	25.9	25.8	28.8	23.0	25.7	23.2	25.1	25.7	27.5	23.9		20.8	
	33	21.4	24.7	23.8	23.2	25.0	23.6	25.6	27.7	29.8	25.0		19.9	
	50	27.5	26.4	26.5	27.8	29.8	21.8	26.3	22.7	31.3	28.8		20.9	
	51	23.3	22.8	23.4	26.4	24.4	19.8	21.7	26.3	29.2	25.0		18.8	
	68	18.4	23.8	24.3	27.2	23.6	19.4	24.1	26.0	27.3	23.5		20.1	
	69	.[e]												
	86	.[e]												
	87	28.5	25.3	25.5	25.3	29.1	20.7	28.0	27.0	27.5	24.1	26.2	22.6	22.7
	104	25.4	27.8	26.6	27.1	26.3	22.5	26.7	27.7	31.9	25.2	27.2	.[d]	.[d]
	105	23.4	25.3	21.9	29.3	26.1	17.9	24.3	26.9	30.7	23.3	25.3	20.8	20.9
	122	19.8	23.1	22.0	27.0	22.7	18.9	27.5	22.0	27.6	20.8	25.0	20.1	20.2
	123	20.8	21.0	23.0	28.3	21.6	19.7	21.9	23.9	27.3	21.0	22.3	19.0	19.1
	135	.[e]												
2	4	22.9	19.9	20.4	.[c]	23.2	23.0	23.1	17.3	21.2	19.7		.[d]	
	18	.[f]												
	29	25.6	22.8	20.7	23.1	23.1	22.1	21.9	22.2	22.3	21.9		19.1	
	36	30.6	24.8	21.8	23.4	23.3	24.7	24.0	24.3	22.2	23.3		19.6	
	47	19.4	20.7	18.4	22.1	20.2	21.9	20.1	21.7	19.2	25.1		18.1	
	54	.[g]												
	65	27.0	25.7	25.8	23.3	27.6	24.5	26.3	27.8	25.7	28.8		20.6	
	72	.[h]	27.3	27.1	28.8	27.8	.[h]	26.3	26.7	29.7	30.7		.[d]	
	83	24.0	23.1	21.6	22.9	23.4	25.0	23.9	28.6	17.0	15.8	21.0	18.9	19.0
	90	24.6	23.0	24.4	26.5	25.3	23.0	27.9	24.9	23.2	24.9	25.1	.[d]	.[d]
	101	23.9	21.3	24.4	22.1	24.8	23.0	23.6	20.7	22.6	23.2	18.8	.[d]	.[d]
	108	25.3	19.9	24.6	26.1	25.2	23.6	23.9	22.5	21.9	27.7	18.3	.[d]	.[d]
	119	.[e]												
	126	22.8	20.1	22.2	22.8	21.7	19.4	22.1	20.3	24.4	25.9	18.2	18.8	18.8
	133	25.2	23.4	22.6	23.8	24.1	23.7	18.0	27.3	23.7	27.3	19.7	20.1	20.1

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 2 of 10)

Group[a]	Animal ID	Postnatal Days												
		42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
3	5	20.1	20.5	19.9	.[c]	18.7	21.7	20.5	22.1	19.9	21.4		.[d]	
	13	18.1	20.5	21.1	.[c]	22.5	17.7	19.6	19.1	18.5	21.9		.[d]	
	19	23.6	22.8	.[h]	.[i]	21.0	22.4	22.8	27.9	22.6	26.3		.[d]	
	28	25.0	23.8	22.6	19.6	24.7	20.1	22.8	25.8	23.9	26.1		18.9	
	37	24.1	18.3	18.6	19.5	19.5	19.5	19.0	21.6	22.6	21.9		.[d]	
	46	21.7	23.5	21.3	21.3	19.7	23.0	21.9	20.8	26.2	24.7		18.0	
	55	.[e]												
	64	.[h]	.[i]	22.0	21.6	20.0	26.5	22.5	23.2	22.6	28.8		.[d]	
	73	23.0	21.6	24.6	23.8	18.6	21.0	22.9	22.4	21.8	26.8		19.1	
	82	24.0	24.0	19.3	19.8	23.4	22.1	26.2	15.4	25.8	23.4	24.6	18.4	18.7
	91	24.8	25.6	23.9	26.9	24.3	23.7	25.5	25.5	24.7	28.8	25.1	.[d]	.[d]
	100	22.8	23.7	23.3	20.6	22.2	23.2	21.0	21.1	24.4	24.6	23.0	18.5	18.7
	109	17.2	21.1	19.2	23.6	17.8	17.8	18.4	19.3	17.4	21.7	20.3	.[d]	.[d]
	118	.[e]												
	127	.[e]												
4	6	21.9	21.4	20.5	.[c]	21.4	21.5	25.0	18.7	23.1	20.2		.[d]	
	12	22.6	24.4	26.7	.[c]	29.4	23.4	24.3	22.5	27.5	30.7		.[d]	
	20	.[j]												
	27	26.9	27.8	27.6	30.1	26.7	29.5	30.2	28.7	29.5	33.0		22.5	
	38	25.1	24.2	24.2	25.7	28.5	23.3	30.3	24.8	24.7	29.1		20.8	
	45	26.2	22.0	26.7	26.8	21.6	27.6	24.4	28.3	24.1	28.1		19.9	
	56	29.5	26.5	26.1	25.9	28.4	28.9	29.4	30.4	28.6	39.5		23.2	
	63	24.7	24.8	24.3	25.8	24.0	25.8	24.5	26.9	26.9	26.9		20.8	
	74	.[e]												
	81	27.0	25.3	28.2	24.0	25.6	25.7	25.0	31.6	30.6	34.4	27.1	.[d]	.[d]
	92	22.8	23.3	23.4	22.2	24.1	20.4	24.5	24.1	24.4	27.0	22.4	19.5	19.6
	99	27.2	26.6	24.8	25.1	27.7	22.2	26.5	27.7	37.5	29.2	31.0	22.2	22.5
	110	24.3	26.4	23.5	.[c]	20.8	22.4	24.4	22.4	33.1	26.3	27.9	.[d]	.[d]
	117	29.6	26.5	.[h]	.[i]	23.4	22.7	24.2	28.3	33.4	26.0	28.2	.[d]	.[d]
	128	23.7	27.0	27.7	26.8	24.3	24.1	26.5	25.7	31.2	26.6	29.3	21.8	22.0

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 3 of 10)

		Postnatal Days												
Group[a]	Animal ID	42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
5	7	.[h]	.[h]	.[i]	.[c]	21.9	23.5	24.4	21.2	29.1	.[h]		.[d]	
	21	31.1	24.0	28.1	28.5	25.1	28.1	28.7	29.1	36.3	25.6		.[d]	
	26	26.6	26.1	29.7	29.1	33.0	25.6	28.0	35.2	36.9	30.9		23.7	
	39	26.3	27.3	23.1	29.4	23.1	24.9	26.7	23.6	33.2	24.0		20.8	
	44	28.2	23.1	24.6	24.4	24.5	24.0	26.2	27.8	34.7	21.7		20.8	
	57	28.0	23.2	26.9	32.3	26.0	25.7	28.5	27.6	35.0	31.4		22.2	
	62	22.6	22.3	20.7	28.4	22.3	20.4	22.1	23.8	29.9	22.9		18.9	
	75	25.5	22.4	23.6	25.8	21.4	22.5	25.3	26.6	33.0	25.6		19.8	
	80	26.9	23.5	25.2	29.7	27.4	27.2	27.3	28.0	33.2	24.6	26.0	20.8	21.0
	93	27.8	24.2	28.0	27.6	29.5	24.7	28.0	30.5	34.9	28.1	33.9	21.8	22.2
	98	25.0	24.6	24.5	26.1	25.5	22.6	26.5	26.7	33.4	21.8	27.0	21.3	21.5
	111	18.4	25.8	27.0	25.2	25.1	23.8	25.1	28.2	29.8	26.6	26.2	21.9	22.0
	116	28.2	28.2	28.3	27.4	25.5	28.2	31.5	29.5	36.8	27.1	29.9	23.6	23.9
	129	25.4	22.2	27.9	25.4	31.1	25.3	28.8	33.4	34.6	26.6	33.2	23.2	23.6
	132	25.7	26.3	26.8	23.8	24.3	26.4	27.3	27.2	30.3	27.5	25.1	21.7	21.8
6	8	22.7	24.8	23.9	.[c]	22.9	23.8	23.3	23.3	27.6	26.7		.[d]	
	11	22.0	23.2	22.9	.[c]	20.2	24.5	22.4	22.9	26.6	21.4		.[d]	
	22	29.1	28.4	31.3	25.1	28.8	29.3	32.5	39.1	37.5	33.1		24.0	
	25	23.9	24.2	23.8	23.8	22.7	26.6	24.4	30.9	31.1	25.5		20.3	
	40	25.6	28.1	26.1	26.1	26.0	25.7	25.8	26.9	33.1	30.2		21.7	
	43	20.1	21.6	21.8	16.8	19.0	19.1	18.6	21.4	22.5	21.0		17.3	
	58	24.3	22.5	21.7	20.0	21.5	23.7	22.3	24.5	29.6	25.7		18.9	
	61	22.5	26.5	22.5	22.7	21.7	22.4	24.1	28.0	24.7	26.5		20.7	
	76	25.7	23.2	19.9	13.4	31.5	22.8	24.7	27.6	30.7	25.6	25.2	19.9	20.1
	79	.[e]												
	94	28.9	26.9	24.3	27.1	24.1	26.3	25.8	25.7	31.8	28.4	27.8	22.5	22.7
	97	25.7	25.7	25.7	26.6	24.2	27.1	28.2	28.4	34.9	26.6	28.4	21.6	21.8
	112	13.6	27.3	27.2	40.1	15.2	29.0	28.1	31.1	33.7	34.4	22.6	.[d]	.[d]
	115	.[e]												
	130	30.1	30.2	29.1	28.2	30.8	29.0	31.5	35.3	43.4	33.9	30.8	.[d]	.[d]

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 4 of 10)

Group[a]	Animal ID	Postnatal Days												
		42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
7	9	23.5	25.9	25.0	.[c]	20.3	25.0	25.1	24.3	28.0	29.0		.[d]	
	10	25.9	26.7	23.4	.[c]	23.3	23.9	25.1	24.0	26.4	28.2		.[d]	
	23	21.2	23.6	23.6	22.9	25.4	22.4	25.3	29.3	21.1	27.7		.[d]	
	24	.[e]												
	41	23.7	24.8	23.1	22.4	22.9	22.7	23.6	23.2	29.1	24.2		20.0	
	42	26.3	24.9	23.9	22.1	23.3	28.6	22.3	24.5	28.9	27.2		20.6	
	59	26.5	22.3	25.5	21.5	21.8	26.1	24.6	25.4	26.8	25.1		20.5	
	60	23.9	22.7	23.2	21.6	23.0	23.3	22.3	28.1	29.4	25.3		19.9	
	77	.[h]	.[h]	21.5	12.9	19.0	24.1	23.9	24.0	25.8	25.5	18.2	.[d]	.[d]
	78	24.6	25.8	22.9	22.1	23.6	25.1	24.4	25.3	31.2	24.1	24.3	.[d]	.[d]
	95	24.3	23.2	28.0	22.3	24.2	21.6	25.9	24.7	29.3	23.8	22.0	20.2	20.3
	96	26.5	28.0	25.4	23.2	27.3	26.1	29.9	28.4	34.1	24.2	27.4	21.8	22.0
	113	28.4	25.1	27.3	24.1	26.3	23.6	26.2	28.1	30.2	28.1	24.3	22.1	22.1
	114	.[e]												
	131	.[e]												
8	2	18.4	19.3	20.6	30.4	26.9	18.0	18.2	23.1	24.8	24.5		17.2	
	16	24.4	27.4	25.5	23.7	26.5	27.6	30.1	25.0	30.5	23.6		21.5	
	31	20.8	20.4	20.9	19.4	23.3	22.7	23.4	23.1	30.2	22.8		17.6	
	34	19.2	21.3	21.6	22.1	22.9	23.6	24.0	23.9	26.7	21.3		18.8	
	49	22.6	26.1	23.4	21.2	26.2	21.4	25.1	24.0	27.5	19.9		19.7	
	52	24.6	28.8	27.5	26.0	29.4	24.8	29.8	28.0	34.3	30.9		24.1	
	67	18.6	19.2	22.5	20.3	21.7	22.5	22.4	21.1	24.9	24.4		18.9	
	70	22.1	24.4	23.0	24.3	23.7	22.8	24.5	27.0	27.9	20.4		20.4	
	85	23.2	25.0	22.0	24.3	26.0	27.2	26.8	25.9	24.8	20.6	27.5	20.7	20.9
	88	18.4	22.4	23.0	21.3	26.3	22.8	22.7	24.5	25.1	20.5	21.9	.[d]	.[d]
	103	23.6	21.3	25.9	22.7	23.3	24.2	24.6	26.3	29.9	20.8	23.8	20.1	20.2
	106	20.5	22.7	21.1	20.0	23.0	23.0	19.3	24.1	21.2	21.3	20.9	18.8	18.9
	121	23.1	22.4	24.4	30.3	17.7	25.5	24.7	23.0	22.5	21.8	30.0	20.1	20.5
	124	22.3	22.2	20.6	17.3	22.7	19.4	21.0	24.2	24.5	18.7	23.4	18.5	18.7
	134	24.6	23.6	25.2	22.8	28.2	23.6	25.8	24.3	25.9	25.2	27.7	.[d]	.[d]

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 5 of 10)

		Postnatal Days												
Group[a]	Animal ID	42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
9	3	17.2	18.2	22.4	.[c]	19.3	18.0	16.5	22.2	19.6	18.2		.[d]	
	14	18.6	19.5	18.7	.[c]	21.9	19.8	17.7	19.3	22.8	21.6		.[d]	
	17	.[e]												
	30	.[e]												
	35	30.0	21.6	.[h]	25.1	26.9	27.4	24.7	23.4	27.4	22.6		.[d]	
	48	24.9	20.0	22.8	24.3	27.4	25.5	25.6	25.6	25.8	23.0		20.6	
	53	24.6	24.5	22.0	22.7	26.8	27.2	26.3	26.2	23.5	24.2		20.5	
	66	22.3	23.0	24.3	24.1	24.4	22.7	21.7	26.2	23.1	21.8		20.5	
	71	21.9	21.0	23.5	22.2	23.8	23.0	23.9	21.9	26.8	21.5		20.3	
	84	23.0	22.3	21.4	23.3	25.1	23.1	23.7	24.0	27.8	20.7	25.2	20.1	20.3
	89	22.7	20.9	23.0	20.9	29.8	25.4	22.9	22.6	27.7	18.6	23.6	19.7	19.9
	102	24.3	20.8	22.4	26.1	24.8	23.5	24.9	26.3	28.8	21.3	28.8	.[d]	.[d]
	107	26.2	24.7	25.7	22.1	24.2	28.1	27.2	28.6	25.3	22.0	25.5	21.6	21.7
	120	25.2	24.5	26.9	25.2	23.9	23.2	25.6	29.2	27.6	22.5	25.0	22.1	22.2
	125	22.1	25.3	27.2	28.7	24.4	25.3	25.2	31.7	28.4	23.3	32.3	21.8	22.2
10	136	21.2	19.5	20.5	20.8	.[h]	.[h]	22.3	21.6	19.0	21.0		.[d]	
	153	21.5	22.9	23.0	24.5	24.0	24.1	23.5	24.3	26.9	25.9		19.3	
	154	26.4	23.7	24.7	24.4	26.2	23.7	24.7	24.5	26.6	26.6		19.9	
	171	23.3	24.9	24.0	24.1	24.8	26.1	23.3	25.1	27.7	26.6		19.8	
	172	24.5	21.5	23.1	22.7	25.2	24.3	21.3	21.0	28.5	23.0		19.9	
	182	26.8	28.4	28.2	31.3	29.1	28.1	33.3	34.5	31.1	31.5		24.0	
	199	16.0	16.3	21.4	25.0	25.5	22.8	28.1	25.7	27.0	28.0		19.6	
	200	27.0	25.4	23.6	29.5	25.9	25.5	30.7	29.3	28.9	26.2		21.5	
	217	.[k]												
	218	22.6	23.9	23.2	22.1	24.2	21.4	21.8	24.1	23.0	22.5		.[d]	
	235	23.9	25.3	23.4	28.3	22.0	25.3	26.5	26.2	28.0	26.5	27.0	21.7	21.9
	236	22.2	24.1	24.7	23.0	22.4	23.3	24.2	24.4	25.1	24.5	26.7	20.2	20.4
	253	24.3	21.8	23.9	23.8	25.7	24.6	25.1	26.8	26.9	25.0	22.9	19.6	19.7
	254	21.5	22.6	22.6	23.2	24.9	23.3	23.1	23.8	25.7	23.6	24.6	19.7	19.9
	270	25.0	23.0	24.6	27.9	23.8	26.8	25.2	30.0	28.0	28.2	28.4	21.4	21.6

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 6 of 10)

Group[a]	Animal ID	Postnatal Days												
		42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
11	137	22.2	18.5	16.0	17.1	17.1	17.6	14.7	17.5	15.9	14.8		16.2	
	152	21.0	22.4	22.8	22.5	22.7	20.8	23.2	20.4	19.3	20.0		19.0	
	155	26.7	21.8	21.5	23.1	19.5	20.4	16.9	19.5	21.0	18.0		19.1	
	170	22.6	21.8	22.6	23.0	22.2	20.5	19.8	19.7	20.5	20.3		.[d]	
	173	29.3	27.0	26.6	27.9	25.0	24.9	30.2	24.7	26.7	27.2		22.7	
	183	23.5	21.5	23.8	21.1	23.4	20.5	22.9	23.4	23.7	18.5		18.5	
	198	26.3	24.1	23.5	23.5	21.6	24.4	22.5	23.0	25.0	20.5		20.5	
	201	23.8	23.0	21.5	24.1	23.7	21.7	22.7	22.2	23.8	20.2		19.5	
	216	25.3	24.0	23.9	23.4	25.7	24.5	24.6	25.9	25.4	21.5		20.5	
	219	19.2	17.3	18.9	18.9	18.8	16.7	16.1	15.0	17.9	13.6		17.5	
	234	21.2	25.7	18.9	22.9	22.0	25.7	18.7	23.0	23.7	20.1	20.3	18.8	18.9
	237	24.2	25.3	21.7	23.3	23.2	20.8	22.9	21.1	21.3	19.0	17.6	20.0	19.9
	252	24.9	23.9	23.1	21.5	22.9	20.4	20.8	19.5	19.6	18.2	18.2	20.1	20.0
	255	22.4	23.1	21.2	23.4	18.7	18.6	19.7	20.6	20.3	17.4	15.9	18.6	18.5
	269	27.6	21.5	23.7	25.0	23.9	23.0	25.8	23.6	25.1	19.7	20.2	20.8	20.7
12	138	11.9	10.1	10.0	10.5	10.9	12.3	7.8	10.6	10.0	10.4		.[d]	
	151	9.4	9.9	8.8	10.1	9.0	9.5	7.7	9.8	9.3	8.7		10.4	
	156	12.7	9.9	10.8	11.3	10.4	10.7	9.6	10.8	10.1	9.4		11.8	
	169	13.6	12.7	11.3	11.6	12.3	11.3	10.8	10.7	10.0	10.3		13.1	
	174	11.8	11.5	10.3	10.4	11.2	11.5	10.2	10.0	9.1	9.3		12.7	
	184	10.6	9.9	9.0	10.5	10.6	8.4	11.6	8.6	10.2	8.0		11.3	
	197	11.6	12.6	11.4	13.0	12.6	12.8	11.7	11.0	12.7	9.9		12.4	
	202	10.6	9.8	10.8	10.7	10.5	9.2	10.6	10.4	9.7	9.8		11.7	
	215	14.5	12.6	15.2	12.1	13.3	14.8	13.1	12.6	12.7	10.4		14.5	
	220	12.4	11.7	11.4	10.6	11.1	11.2	11.6	11.8	11.0	8.9		13.3	
	233	12.0	10.6	.[h]	.[i]	12.4	10.9	12.6	10.5	11.0	9.9	9.5	.[d]	.[d]
	238	12.7	12.2	11.9	11.1	11.1	11.9	12.1	12.4	10.7	10.1	8.7	13.8	13.6
	251	14.1	12.1	12.8	12.8	12.3	10.4	13.4	12.1	13.8	10.0	10.3	13.3	13.2
	256	13.9	10.3	14.3	11.2	11.6	10.7	11.5	11.8	11.5	9.0	10.3	13.5	13.4
	268	12.1	11.2	11.4	11.0	10.0	9.4	10.5	.[l]					

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 7 of 10)

		Postnatal Days												
Group[a]	Animal ID	42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
13	141	26.3	16.3	24.0	17.7	30.8	25.9	24.1	20.1	27.9	23.5		.[d]	
	148	28.4	26.4	25.2	25.8	25.6	26.5	26.0	28.6	27.9	29.5		21.7	
	159	22.9	22.4	19.9	22.0	21.7	21.9	21.9	20.8	25.4	23.8		17.9	
	166	26.8	26.8	24.3	26.1	25.9	28.4	25.7	30.0	24.6	.[h]		.[d]	
	177	29.6	27.1	27.5	25.3	28.3	27.2	28.1	25.9	28.3	28.2		22.4	
	187	23.4	25.1	23.5	27.2	24.5	26.3	26.5	26.6	29.8	26.6		20.8	
	194	23.1	23.1	23.0	22.0	17.7	27.2	23.5	22.5	22.8	22.7		18.6	
	205	26.0	23.3	24.7	25.4	25.4	27.0	24.5	28.0	29.5	27.2		21.2	
	212	25.1	23.8	25.6	22.0	27.4	23.5	25.6	26.0	26.9	24.8		20.9	
	223	25.0	22.1	24.5	25.8	27.9	27.7	25.6	28.3	26.9	28.6		21.8	
	230	22.5	24.8	24.0	21.3	29.1	21.0	25.8	26.8	25.2	24.6	28.0	19.7	20.0
	241	27.5	26.7	24.1	25.2	27.5	24.0	28.1	28.8	28.3	26.6	26.9	22.9	23.0
	248	27.0	24.6	24.5	25.4	29.1	23.5	27.6	27.3	29.6	29.7	28.0	21.0	21.3
	259	24.4	23.5	26.1	23.2	25.6	24.0	24.3	26.5	27.4	25.1	25.3	21.3	21.4
	265	21.0	29.1	22.9	29.3	28.4	25.2	28.3	30.0	31.0	26.3	27.6	23.0	23.1
14	142	21.8	20.6	20.9	20.7	19.9	21.9	19.3	20.7	23.0	21.3		17.3	
	147	30.0	19.6	25.0	26.4	21.8	21.1	21.7	21.8	27.2	20.1		19.1	
	160	18.2	25.5	23.1	22.6	22.3	26.1	24.5	24.5	26.9	22.1		19.1	
	165	21.6	24.5	22.8	20.4	23.8	23.2	22.0	25.2	23.8	22.6		18.2	
	178	26.1	27.2	23.4	26.8	26.1	23.3	28.7	28.8	26.1	29.1		21.2	
	188	23.0	24.1	23.0	23.8	25.3	24.0	22.6	26.9	25.6	24.3		.[d]	
	193	22.3	22.9	22.1	21.1	25.4	19.7	21.3	26.5	23.8	23.4		.[d]	
	206	22.3	24.5	21.6	19.8	26.9	22.7	25.6	27.7	25.2	25.0		.[d]	
	211	15.6	20.0	18.8	20.3	26.1	19.3	21.1	25.5	25.0	20.7		18.0	
	224	24.9	24.6	20.2	24.0	25.0	21.9	22.6	26.3	25.3	20.0		19.9	
	229	28.4	28.4	23.3	27.6	29.0	24.7	27.9	28.5	31.6	30.0	24.9	.[d]	.[d]
	242	.[m]												
	247	28.8	26.0	25.4	28.5	27.3	29.7	30.0	28.9	29.1	28.3	28.7	.[d]	.[d]
	260	27.0	27.3	27.2	27.8	28.3	25.4	30.7	28.7	32.2	27.7	30.6	22.7	23.0
	264	24.4	26.0	22.9	27.2	30.1	22.3	27.4	28.5	31.8	22.2	29.6	22.1	22.4

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 8 of 10)

		Postnatal Days												
Group[a]	Animal ID	42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
15	139	21.9	24.0	19.6	27.0	20.5	24.7	22.0	22.9	23.8	27.8		18.3	
	150	24.2	23.7	21.1	23.4	23.2	24.5	26.8	24.5	24.4	24.7		18.6	
	157	24.7	23.5	23.9	24.2	25.3	22.9	27.4	25.5	26.3	25.2		19.1	
	168	21.8	24.5	13.8	.[h]	23.8	24.0	23.8	25.1	25.0	25.9		.[d]	
	175	22.9	23.1	22.8	23.2	24.2	24.5	21.7	26.0	25.4	25.9		19.0	
	185	23.6	24.4	23.8	22.8	22.1	21.8	26.3	24.5	23.8	21.2		19.1	
	196	25.4	21.1	25.5	24.3	24.1	25.1	25.3	25.5	27.7	22.9		19.2	
	203	25.0	22.8	25.6	22.1	26.1	24.3	26.2	27.3	26.5	24.3		20.0	
	214	24.0	22.3	20.9	22.3	26.4	21.3	23.1	26.6	24.5	21.2		18.1	
	221	22.5	24.7	25.0	25.4	22.1	27.6	23.5	22.7	24.6	26.0		19.0	
	232	22.8	22.8	22.9	24.6	22.2	23.5	22.8	24.3	25.6	24.0	23.1	18.6	18.7
	239	20.2	22.0	24.9	24.5	27.1	27.7	27.1	25.6	26.8	26.6	28.7	20.0	20.3
	250	20.8	22.0	24.4	24.1	21.4	23.3	25.0	19.8	23.2	21.7	24.5	18.3	18.5
	257	26.8	26.3	29.4	28.4	25.0	29.8	26.6	28.3	29.0	30.7	26.3	22.5	22.6
	267	24.5	25.6	24.4	25.0	23.9	26.5	25.3	27.7	27.4	28.5	26.7	20.4	20.6
16	140	20.7	22.4	22.4	23.4	23.7	23.0	22.5	18.9	22.2	21.1		17.9	
	149	19.4	13.9	18.5	19.1	18.3	19.0	19.4	18.2	20.4	18.4		.[d]	
	158	19.9	20.0	19.6	20.7	21.0	20.5	20.5	18.8	21.7	23.5		17.1	
	167	16.7	18.4	17.6	17.6	22.4	18.4	18.8	19.5	17.1	19.1		14.2	
	176	24.5	25.5	24.1	24.9	27.5	24.8	24.5	22.8	26.8	25.9		19.8	
	186	26.3	22.8	23.2	22.4	25.4	26.1	25.2	26.7	27.3	25.3		19.6	
	195	21.6	20.6	19.0	18.8	23.6	19.7	19.5	21.8	22.7	16.0		17.5	
	204	16.4	19.2	19.5	18.5	22.8	22.8	19.3	18.2	20.8	20.3		16.2	
	213	25.5	21.2	.[i]	.[h]	24.9	24.8	24.2	30.3	25.2	28.8		.[d]	
	222	21.1	21.6	21.4	20.6	21.7	21.5	17.1	22.1	22.3	17.7		17.5	
	231	19.7	18.0	22.5	19.5	18.7	19.6	20.7	20.7	19.2	17.5	20.3	15.4	15.6
	240	23.0	17.5	23.1	23.3	24.7	22.7	22.8	21.9	27.0	25.9	26.1	19.2	19.4
	249	21.3	18.3	22.6	22.8	21.2	20.8	23.4	23.8	23.0	21.8	24.4	17.1	17.4
	258	21.3	22.6	22.6	21.0	21.7	23.8	23.7	22.6	25.2	22.1	20.5	19.8	19.8
	266	20.1	22.1	21.3	22.4	24.3	23.3	24.3	21.8	22.8	20.8	24.6	18.9	19.1

(continued)

Table A-7. Individual F_1 Male Post Wean Feed Consumption (g/day) for Postnatal Days 42 Through 53 (page 9 of 10)

		Postnatal Days												
Group[a]	Animal ID	42-43	43-44	44-45	45-46	46-47	47-48	48-49	49-50	50-51	51-52	52-53[b]	23-52	23-53[b]
17	143	25.4	23.2	25.1	20.7	23.6	19.9	21.0	.[h]	.[i]	26.6		.[d]	
	146	24.1	25.1	29.1	26.8	23.5	28.2	23.4	26.3	28.9	25.1		20.2	
	161	37.5	.[h]	23.6	24.7	26.4	28.9	24.5	21.9	31.7	25.9		.[d]	
	164	29.1	27.8	30.2	27.4	26.7	28.3	25.5	26.4	31.3	27.4		22.2	
	179	18.7	22.4	24.3	24.5	25.2	24.3	25.9	23.7	24.5	26.5		21.3	
	189	27.6	24.2	24.8	27.2	25.3	25.0	24.3	26.6	28.1	22.5		20.4	
	192	25.9	26.3	26.5	27.6	26.9	22.8	26.8	31.5	28.1	22.1		22.5	
	207	22.5	21.5	26.2	22.5	22.4	21.3	24.9	24.7	25.8	25.8		20.0	
	210	22.5	22.6	21.4	24.5	22.2	21.6	21.5	24.6	24.2	21.8		18.5	
	225	22.9	28.5	23.2	31.1	27.9	26.3	27.3	28.5	32.0	23.7		.[d]	
	228	24.5	23.4	24.9	24.0	26.3	22.2	24.8	26.3	25.3	25.9	24.3	20.5	20.6
	243	27.0	32.8	25.1	32.8	37.2	31.7	33.8	35.2	34.4	37.6	36.5	25.4	25.8
	246	21.8	21.2	23.0	24.0	22.5	21.3	22.3	22.3	22.1	22.1	21.9	18.9	19.0
	261	21.1	26.8	25.5	25.6	26.0	25.4	24.0	28.6	25.5	27.4	27.0	20.7	20.9
	263	24.9	24.3	24.1	20.7	25.0	24.5	22.2	24.3	25.4	25.0	24.8	20.3	20.4
18	144	23.1	21.7	23.2	21.0	23.8	21.0	21.9	23.5	23.5	23.5		18.4	
	145	25.1	26.1	25.2	28.1	24.7	24.4	20.9	24.8	24.7	21.6		20.1	
	162	24.6	23.7	25.4	24.0	26.8	25.9	23.2	23.8	27.8	22.5		19.3	
	163	25.2	25.0	26.7	24.9	27.2	27.1	24.6	25.7	28.0	25.0		20.7	
	180	23.7	22.1	23.2	24.0	25.1	23.3	24.0	24.9	23.2	23.6		19.3	
	181	22.2	21.4	23.0	22.6	22.8	22.5	19.8	21.9	22.7	21.6		18.1	
	190	20.6	20.5	17.1	22.5	27.6	19.1	23.2	23.3	24.5	22.5		19.3	
	191	22.0	22.9	19.6	24.8	26.2	27.9	24.9	26.1	24.4	23.6		19.4	
	208	21.8	22.9	21.7	25.0	27.0	22.8	25.9	26.7	35.1	15.0		20.2	
	209	27.6	24.9	26.3	28.6	27.0	25.9	27.3	28.9	29.2	24.3		22.4	
	226	29.3	29.4	29.9	30.0	28.7	30.8	33.3	33.1	31.6	29.0		24.2	
	227	27.0	26.1	24.7	27.9	24.7	25.0	27.9	24.9	27.3	25.0		21.3	
	244	29.6	25.3	27.2	26.8	31.4	25.9	30.8	31.1	29.2	28.6	31.1	22.8	23.1
	245	22.4	27.2	23.3	26.0	28.3	25.3	24.9	29.1	30.4	25.0	25.8	21.4	21.5
	262	22.4	23.2	24.2	22.8	24.1	25.4	25.2	26.0	25.5	24.4	24.6	.[d]	.[d]

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.
[b]Includes only those animals scheduled for necropsy on postnatal day 53.
[c]Feed weight inadvertently not recorded.
[d]Interim feed consumption value(s) are missing and therefore this overall value could not be calculated.
[e]Male was removed from the study because his correct postnatal day 0 could not be confirmed.
[f]Male was removed from the study because it was not dosed on the correct postnatal days.
[g]Male was found dead on postnatal day 37 after dosing (misdirected dose).
[h]Feed consumption value was excluded because it was a statistical outlier.
[i]Feed consumption value was excluded because it was unrealistic (i.e. negative).
[j]Male was euthanized on postnatal day 29 after dosing due to a leg injury.
[k]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).
[l]Male was found dead on postnatal day 50 prior to dosing.
[m]Male was found dead on postnatal day 37 prior to dosing (misdirected dose).

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 1 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
1	50	47	Salivation: prior to dosing
	68	47	Salivation: prior to dosing
2	29	45	Rooting: post dosing
	36	29	Salivation: prior to dosing
		30	Salivation: prior to dosing
		31	Salivation: prior to dosing
		32	Salivation: prior to dosing
		33	Salivation: prior to dosing
		34	Salivation: prior to dosing
		35	Salivation: prior to dosing
		36	Salivation: prior to dosing
		37	Salivation: prior to dosing
			Efflux of the dosing solution
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
			Rooting: post dosing
		47	Salivation: prior to dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
			Rooting: post dosing
		50	Salivation: prior to dosing
		51	Rooting: post dosing
	47	33	Salivation: prior to dosing
		34	Salivation: prior to dosing
		35	Salivation: prior to dosing
		36	Salivation: prior to dosing
		38	Salivation: prior to dosing
		42	Salivation: prior to dosing
		50	Efflux of the dosing solution, small amount
	54	33	Salivation: prior to dosing
		37	Salivation: prior to dosing
			Found dead after dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 2 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
2	65	37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		41	Salivation: prior to dosing
		44	Salivation: prior to dosing
		46	Salivation: prior to dosing
		50	Salivation: prior to dosing
	72	37	Salivation: prior to dosing
		39	Efflux of the dosing solution, slight
		41	Salivation: prior to dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
		46	Salivation: prior to dosing
			Rooting: post dosing
		47	Salivation: prior to dosing
			Efflux of the dosing solution
			Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
		50	Rooting: post dosing
	90	25	Efflux of the dosing solution
		39	Rooting: post dosing
	108	38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
		41	Salivation: prior to dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing
		45	Salivation: prior to dosing
		46	Salivation: prior to dosing
		47	Salivation: prior to dosing
		49	Salivation: prior to dosing
		50	Salivation: prior to dosing
		51	Salivation: prior to dosing
	126	38	Salivation: prior to dosing
		39	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 3 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
2	133	33	Salivation: prior to dosing
		34	Salivation: prior to dosing
		35	Salivation: prior to dosing
		37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		52	Rooting: post dosing
3	5	34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		45	Salivation: prior to dosing
		46	Rooting: post dosing
	13	24	Efflux of the dosing solution
		31	Salivation: prior to dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		36	Rooting: post dosing
		37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
			Efflux of the dosing solution
			Rooting: post dosing
		40	Salivation: prior to dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Salivation: prior to dosing
		44	Salivation: prior to dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
			Rooting: post dosing
		47	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 4 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
3	13	48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
			Rooting: post dosing
		50	Salivation: prior to dosing
			Rooting: post dosing
	19	29	Salivation: prior to dosing
			Rooting: post dosing
		30	Salivation: prior to dosing
		32	Salivation: prior to dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		34	Rooting: prior to dosing
			Salivation: prior to dosing
			Rooting: post dosing
		35	Rooting: prior to dosing
			Salivation: prior to dosing
			Rooting: post dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
			Rooting: post dosing
		47	Salivation: prior to dosing
			Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
			Rooting: post dosing
		51	Salivation: prior to dosing
	28	37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 5 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
3	28	41	Salivation: prior to dosing
		42	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Salivation: prior to dosing
		49	Salivation: prior to dosing
		50	Salivation: prior to dosing
		51	Salivation: prior to dosing
	37	30	Rooting: post dosing
		32	Salivation: prior to dosing
		33	Salivation: prior to dosing
		34	Salivation: prior to dosing
		35	Salivation: prior to dosing
		36	Salivation: prior to dosing
		37	Salivation: prior to dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Salivation: prior to dosing
		46	Salivation: prior to dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
			Rooting: post dosing
		50	Salivation: prior to dosing
			Rooting: post dosing
		51	Salivation: prior to dosing
	46	33	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
		44	Rooting: post dosing
			Salivation: post dosing
		45	Salivation: prior to dosing
		46	Salivation: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 6 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
3	46	47	Rooting: post dosing
			Salivation: post dosing
		48	Salivation: prior to dosing
			Rust colored fur: chin
			Rooting: post dosing
		49	Salivation: prior to dosing
			Rust colored fur: chin
			Rooting: post dosing
		50	Salivation: prior to dosing
			Rust colored fur: chin
			Rooting: post dosing
	64	45	Salivation: prior to dosing
	73	38	Rooting: post dosing
		41	Rooting: post dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Salivation: prior to dosing
			Rooting: prior to dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
	82	37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
			Rooting: post dosing
		47	Salivation: prior to dosing
			Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 7 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
3	82	49	Salivation: prior to dosing
			Rooting: post dosing
		52	Salivation: prior to dosing
			Rooting: post dosing
	91	32	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		37	Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		40	Rooting: post dosing
		42	Salivation: prior to dosing
		44	Rooting: post dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		48	Rooting: post dosing
		52	Salivation: prior to dosing
			Rooting: post dosing
	100	32	Rooting: post dosing
		35	Rooting: post dosing
		43	Salivation: prior to dosing
			Efflux of the dosing solution
		44	Rooting: post dosing
		50	Efflux of the dosing solution
	109	32	Rooting: post dosing
		35	Salivation: prior to dosing
		36	Salivation: prior to dosing
		37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		41	Salivation: prior to dosing
		42	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Rooting: post dosing
		45	Salivation: prior to dosing
		49	Rooting: post dosing
		50	Rooting: post dosing
		51	Rooting: post dosing
		52	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 8 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
4	20	26	Injury of the left rear leg, swelling of the left metatarsal area, possible fracture but not evident
		27	Injury of the left rear leg, swelling of the left metatarsal area, possible fracture but not evident
		28	Injury of the left rear leg, swelling of the left metatarsal area, possible fracture but not evident
		29	Injury of the left rear leg, increased swelling of the left metatarsal area, possible fracture but not evident
			Euthanized after dosing due to a leg injury
	81	43	Rust colored fur: back
		44	Rust colored fur: back
	110	29	Rooting: post dosing
			Salivation: prior to dosing
		31	Salivation: prior to dosing
		32	Salivation: prior to dosing
			Rooting: post dosing
		34	Salivation: prior to dosing
		35	Salivation: prior to dosing
			Rooting: post dosing
		37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
		41	Salivation: prior to dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
		45	Salivation: prior to dosing
		47	Salivation: prior to dosing
		49	Salivation: prior to dosing
	117	34	Chromodacryorrhea: nose
5	7	35	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
	21	37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		43	Rooting: post dosing
		45	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 9 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
5	57	26	Efflux of the dosing solution
		35	Rooting: post dosing
		43	Efflux of the dosing solution, slight
	62	35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		40	Salivation: prior to dosing
		49	Rooting: post dosing
	80	41	Rooting: post dosing
	93	35	Rooting: post dosing
	111	35	Rooting: post dosing
		44	Chromodacryorrhea: eye, right
		45	Chromodacryorrhea: eye, right
		46	Chromodacryorrhea: eye, right
		47	Chromodacryorrhea: eye, right
		48	Chromodacryorrhea: eye, right, gone
	116	43	Rooting: post dosing
		45	Rooting: post dosing
	132	29	Rooting: post dosing
		31	Salivation: prior to dosing
			Rooting: post dosing
6	25	39	Efflux of the dosing solution, slight
	40	41	Rooting: post dosing
		44	Rooting: post dosing
	43	43	Rooting: post dosing
	61	35	Rooting: post dosing
		46	Sore(s): neck
		47	Sore(s): neck
		48	Sore(s): neck
		49	Sore(s): neck
		50	Sore(s): neck, healed
	76	37	Salivation: prior to dosing
		38	Salivation: prior to dosing
	97	36	Salivation: prior to dosing
		43	Rooting: post dosing
	112	50	Animal not dosed, no dosing solution available
	130	50	Animal not dosed, no dosing solution available

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 10 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
7	9	29	Salivation: prior to dosing
		30	Salivation: prior to dosing
		32	Salivation: prior to dosing
		33	Salivation: prior to dosing
		34	Salivation: prior to dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
		45	Salivation: prior to dosing
	42	34	Salivation: prior to dosing
		35	Salivation: prior to dosing
		36	Salivation: prior to dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing
	60	37	Salivation: prior to dosing
		38	Salivation: prior to dosing
		40	Salivation: prior to dosing
		45	Salivation: prior to dosing
		51	Salivation: prior to dosing
	77	25	Efflux of the dosing solution
	78	29	Salivation: prior to dosing
			Efflux of the dosing solution
		38	Efflux of the dosing solution, slight
		40	Rooting: post dosing
	95	44	Rooting: post dosing
	96	30	Salivation: prior to dosing
		39	Salivation: prior to dosing
		41	Salivation: prior to dosing
	113	25	Efflux of the dosing solution
			Piloerection
		26	Rooting: post dosing
		45	Rooting: post dosing
		46	Efflux of the dosing solution
			Rooting: post dosing
		49	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 11 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
8	31	34	Chromodacryorrhea: nose
	121	23	Efflux of the dosing solution
	134	23	Efflux of the dosing solution
9	3	23	Efflux of the dosing solution
	71	44	Rooting: post dosing
		45	Rooting: post dosing
		48	Rooting: post dosing
	89	30	Rooting: post dosing
10	217	31	Found dead prior to dosing
11	170	32	Rooting: post dosing
	173	30	Rough coat
	183	39	Rooting: post dosing
	234	38	Efflux of the dosing solution
	237	35	Salivation: prior to dosing
12	138	32	Rooting: post dosing
		34	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
	151	41	Rooting: post dosing
	169	33	Rooting: post dosing
		34	Rooting: post dosing
		36	Rooting: post dosing
		39	Rooting: post dosing
		41	Rooting: post dosing
		43	Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
		49	Rooting: post dosing
	174	34	Rooting: post dosing
		41	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 12 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
12	184	31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		45	Rooting: post dosing
		48	Rooting: post dosing
	197	30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		44	Rooting: post dosing
		45	Efflux of the dosing solution
			Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		50	Efflux of the dosing solution
			Rooting: post dosing
	202	30	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
	215	30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		44	Rooting: post dosing
		47	Rooting: post dosing
	220	30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		37	Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 13 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
12	220	44	Salivation: prior to dosing
			Rooting: post dosing
		45	Rooting: post dosing
		47	Rooting: post dosing
		48	Salivation: prior to dosing
	233	33	Rooting: post dosing
		34	Rooting: post dosing
		41	Rooting: post dosing
		47	Rooting: post dosing
	238	33	Rooting: post dosing
		48	Rooting: post dosing
		51	Rooting: post dosing
	251	30	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
	256	33	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		48	Rooting: post dosing
	268	33	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
		50	Found dead prior to dosing
13	141	31	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		46	Rooting: post dosing
		48	Rooting: post dosing
	148	31	Rooting: post dosing
		35	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		46	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 14 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
13	159	27	Rooting: post dosing
		28	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Salivation: prior to dosing
	166	27	Rooting: post dosing
		28	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
	177	36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
	187	34	Salivation: prior to dosing
		35	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
	194	37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		45	Rooting: post dosing
	205	24	Efflux of the dosing solution
	212	27	Rooting: post dosing
	223	32	Rooting: post dosing
		33	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		44	Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
	230	37	Rooting: post dosing
		38	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 15 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
13	241	30	Rooting: post dosing
		34	Rough coat
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
	248	39	Rooting: post dosing
		40	Rooting: post dosing
		41	Salivation: prior to dosing
		44	Salivation: prior to dosing
		50	Rooting: post dosing
	259	37	Rooting: post dosing
	265	27	Rooting: post dosing
		31	Rooting: prior to dosing
		47	Rooting: post dosing
14	142	27	Rooting: post dosing
		28	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		42	Rooting: post dosing
		46	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
		50	Rooting: post dosing
	147	26	Rooting: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		30	Rough coat
		31	Rooting: post dosing
		32	Rooting: post dosing
		35	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
		47	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 16 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
14	160	26	Rooting: post dosing
		27	Salivation: prior to dosing
			Rooting: post dosing
		28	Salivation: prior to dosing
		29	Rough coat
		30	Rough coat
		32	Salivation: prior to dosing
			Rough coat
		33	Salivation: prior to dosing
			Rooting: post dosing
			Rough coat
		34	Salivation: prior to dosing
			Rough coat
			Rooting: post dosing
		35	Salivation: prior to dosing
			Rough coat
		36	Salivation: prior to dosing
			Rough coat
		37	Salivation: prior to dosing
			Rough coat
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rough coat
			Rooting: post dosing
		39	Salivation: prior to dosing
			Rough coat
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rough coat
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
			Rooting: post dosing
		47	Salivation: prior to dosing
			Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 17 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
14	160	49	Salivation: prior to dosing
		50	Salivation: prior to dosing
			Rooting: post dosing
		51	Salivation: prior to dosing
	165	26	Rooting: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		35	Rooting: post dosing
		36	Piloerection
			Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		43	Rooting: post dosing
		45	Rooting: post dosing
		48	Rooting: post dosing
	178	26	Rooting: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		33	Rooting: post dosing
		38	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		43	Rooting: post dosing
		48	Rooting: post dosing
	188	34	Salivation: prior to dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		44	Rooting: post dosing
	193	26	Rooting: post dosing
		27	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 18 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
14	193	39	Rooting: post dosing
		41	Rooting: post dosing
		46	Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
	206	31	Rooting: post dosing
		32	Rooting: post dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		44	Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		50	Rooting: post dosing
		51	Rooting: post dosing
	211	26	Rooting: post dosing
		27	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		45	Rooting: post dosing
		47	Rooting: post dosing
		50	Rooting: post dosing
		51	Rooting: post dosing
	224	31	Rooting: post dosing
	229	26	Rooting: post dosing
		27	Rooting: post dosing
		33	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 19 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
14	229	36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		44	Rooting: post dosing
		45	Rooting: post dosing
		47	Salivation: prior to dosing
		48	Salivation: prior to dosing
		50	Salivation: prior to dosing
		51	Salivation: prior to dosing
		52	Salivation: prior to dosing
	242	25	Efflux of the dosing solution
		26	Rooting: post dosing
		27	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		36	Salivation: prior to dosing
		37	Found dead prior to dosing
	247	25	Salivation: prior to dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
	260	26	Rooting: post dosing
		27	Rooting: post dosing
		32	Salivation: prior to dosing
			Rooting: post dosing
		34	Salivation: prior to dosing
		37	Rooting: post dosing
		38	Salivation: prior to dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		45	Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
	264	34	Salivation: prior to dosing
		36	Salivation: prior to dosing
		37	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 20 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
14	264	38	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
		41	Salivation: prior to dosing
		45	Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
		50	Salivation: prior to dosing
		51	Salivation: prior to dosing
		52	Salivation: prior to dosing
15	139	31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
		45	Salivation: prior to dosing
		46	Salivation: prior to dosing
			Rooting: post dosing
		47	Salivation: prior to dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
			Rooting: post dosing
		50	Salivation: prior to dosing
			Rooting: post dosing
	150	33	Rooting: post dosing
		34	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 21 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
15	150	43	Rooting: post dosing
		44	Rooting: post dosing
		45	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
		50	Rooting: post dosing
	157	31	Rooting: post dosing
		32	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		41	Rooting: post dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
			Rooting: post dosing
		44	Rooting: post dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
		50	Rooting: post dosing
	168	31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		43	Rooting: post dosing
		45	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 22 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
15	175	31	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		41	Rooting: post dosing
		43	Rooting: post dosing
		45	Rooting: post dosing
		49	Rooting: post dosing
	185	30	Rooting: post dosing
		33	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		44	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
	196	33	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		44	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		51	Rooting: post dosing
	203	33	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		44	Rooting: post dosing
		51	Salivation: post dosing
			Rooting: post dosing
	214	32	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		37	Rooting: post dosing
		39	Rooting: post dosing
		44	Rooting: post dosing
		45	Salivation: prior to dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 23 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
15	221	31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		44	Rooting: post dosing
		45	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		51	Rooting: post dosing
	232	30	Rooting: post dosing
		31	Rooting: post dosing
		33	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		51	Rooting: post dosing
	239	30	Salivation: prior to dosing
		32	Salivation: prior to dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Salivation: prior to dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		51	Rooting: post dosing
	250	33	Rooting: post dosing
		37	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		51	Rooting: post dosing
	257	30	Salivation: prior to dosing
			Rooting: post dosing
		31	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 24 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
15	257	32	Rooting: post dosing
		33	Rooting: post dosing
		34	Salivation: prior to dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		51	Rooting: post dosing
	267	30	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		40	Rooting: post dosing
		41	Salivation: prior to dosing
		42	Salivation: prior to dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
		47	Salivation: prior to dosing
			Rooting: post dosing
		48	Salivation: prior to dosing
		51	Salivation: prior to dosing
16	140	25	Efflux of the dosing solution
		27	Rooting: post dosing
		28	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
			Salivation: prior to dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		34	Salivation: prior to dosing
		35	Rooting: post dosing
		36	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 25 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
16	140	37	Rooting: post dosing
		38	Rooting: post dosing
			Salivation: prior to dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Rooting: post dosing
		49	Rooting: post dosing
	149	27	Rooting: post dosing
		28	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		38	Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Rooting: post dosing
			Difficult to dose
		42	Rooting: post dosing
		45	Rooting: post dosing
	158	27	Rooting: post dosing
		28	Rooting: post dosing
		31	Salivation: prior to dosing
			Rooting: post dosing
		32	Rooting: post dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Salivation: prior to dosing
			Rooting: post dosing
		43	Salivation: prior to dosing
		45	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
		47	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 26 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
16	158	48	Salivation: prior to dosing
			Rooting: post dosing
		49	Salivation: prior to dosing
			Rooting: post dosing
		50	Rooting: post dosing
		51	Rooting: post dosing
	167	27	Rooting: post dosing
		28	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		43	Rooting: post dosing
		45	Rooting: post dosing
	176	26	Rooting: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		29	Rooting: post dosing
		30	Salivation: prior to dosing
		31	Rooting: post dosing
		33	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Salivation: prior to dosing
			Rooting: post dosing
		44	Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
		50	Rooting: post dosing
	186	25	Rooting: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 27 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
16	186	31	Rooting: post dosing
		32	Salivation: prior to dosing
			Rooting: post dosing
		33	Salivation: prior to dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		37	Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
		42	Salivation: prior to dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Salivation: prior to dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		50	Rooting: post dosing
	195	25	Rooting: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Salivation: prior to dosing
			Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Rooting: post dosing
		41	Rooting: post dosing
		44	Rooting: post dosing
		45	Rooting: post dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
	204	26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 28 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
16	204	33	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Rooting: post dosing
		44	Rooting: post dosing
		46	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		50	Rooting: post dosing
		51	Rooting: post dosing
	213	25	Rooting: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		30	Salivation: prior to dosing
			Rooting: post dosing
		31	Rooting: post dosing
		32	Salivation: prior to dosing
			Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		48	Rooting: post dosing
		50	Rooting: post dosing
	222	25	Rooting: post dosing
		26	Salivation: prior to dosing
			Rooting: post dosing
		27	Rooting: post dosing
		29	Salivation: prior to dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 29 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
16	222	34	Rooting: post dosing
		35	Rooting: post dosing
		36	Salivation: prior to dosing
			Rooting: post dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		45	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		50	Rooting: post dosing
		51	Rooting: post dosing
	231	26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing
		31	Salivation: prior to dosing
			Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
		44	Rooting: post dosing
		45	Salivation: prior to dosing
		46	Salivation: prior to dosing
		47	Salivation: prior to dosing
		48	Salivation: prior to dosing
			Rooting: post dosing
		51	Rooting: post dosing
		52	Salivation: prior to dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 30 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
16	240	25	Rooting: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		29	Salivation: prior to dosing
		30	Salivation: prior to dosing Rooting: post dosing
		31	Salivation: prior to dosing Rooting: post dosing
		32	Salivation: prior to dosing Rooting: post dosing
		33	Salivation: prior to dosing Rooting: post dosing
		34	Rooting: post dosing
		35	Salivation: prior to dosing
		36	Rooting: post dosing
		37	Salivation: prior to dosing Rooting: post dosing
		38	Salivation: prior to dosing Rooting: post dosing
		39	Salivation: prior to dosing Rooting: post dosing
		40	Salivation: prior to dosing Rooting: post dosing
		41	Salivation: prior to dosing Rooting: post dosing
		42	Salivation: prior to dosing Rooting: post dosing
		43	Salivation: prior to dosing
		44	Salivation: prior to dosing Rooting: post dosing
		45	Salivation: prior to dosing Rooting: post dosing
		46	Salivation: prior to dosing
		47	Salivation: prior to dosing
		50	Salivation: prior to dosing
		51	Salivation: prior to dosing Rooting: post dosing
	249	26	Rooting: post dosing
		27	Rooting: post dosing
		29	Salivation: prior to dosing
		30	Salivation: prior to dosing Rooting: post dosing
		31	Rooting: post dosing
		32	Salivation: prior to dosing Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 31 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
16	249	33	Salivation: prior to dosing
			Rooting: post dosing
		36	Rooting: post dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
		42	Salivation: prior to dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
		46	Salivation: prior to dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
	258	26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Salivation: prior to dosing
		44	Salivation: prior to dosing
			Rooting: post dosing
	266	26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		44	Rooting: post dosing
		47	Rooting: post dosing
		48	Rooting: post dosing
		50	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 32 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
17	143	25	Ataxia: post dosing
	161	24	Prone: post dosing
		50	Salivation: prior to dosing
	164	27	Rooting: post dosing
		28	Rooting: post dosing
		35	Rough coat
			Rooting: post dosing
		36	Rough coat
		38	Rough coat
			Rooting: post dosing
		39	Rough coat
			Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		49	Rooting: post dosing
	179	24	Ataxia: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
	189	24	Ataxia: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
	192	33	Rough coat
		40	Rooting: post dosing
		41	Rooting: post dosing
		47	Rooting: post dosing
	207	23	Ataxia: post dosing
		24	Prone: post dosing
		33	Rough coat
			Rooting: post dosing
		34	Rough coat
			Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		41	Rooting: post dosing
	210	31	Rooting: post dosing
		34	Rooting: post dosing
		36	Rooting: post dosing
		39	Salivation: prior to dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		48	Salivation: prior to dosing
			Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 33 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
17	225	23	Ataxia: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		41	Rooting: post dosing
	228	23	Prone: post dosing
		24	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		31	Rooting: post dosing
		33	Rooting: post dosing
		34	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
	243	24	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
	246	23	Efflux of the dosing solution
		24	Ataxia: post dosing
		26	Salivation: prior to dosing
			Rooting: post dosing
		27	Salivation: prior to dosing
			Rooting: post dosing
		28	Rooting: post dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Salivation: prior to dosing
			Rooting: post dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		34	Salivation: prior to dosing
			Rough coat
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 34 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
17	246	40	Salivation: prior to dosing
			Rooting: post dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		42	Rooting: post dosing
		43	Rooting: post dosing
		45	Rooting: post dosing
		47	Rooting: post dosing
		51	Rooting: post dosing
	261	31	Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
	263	30	Rooting: post dosing
		48	Rooting: post dosing
18	144	24	Prone: post dosing
		25	Prone: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		32	Rooting: post dosing
		35	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		46	Rooting: post dosing
		48	Rooting: post dosing
	145	24	Ataxia: post dosing
			Prone: post dosing
		25	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		32	Rooting: post dosing
		37	Rough coat
			Rooting: post dosing
		38	Rough coat
			Rooting: post dosing
		39	Rough coat
			Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 35 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
18	162	24	Prone: post dosing
		25	Prone: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		32	Salivation: prior to dosing
		33	Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		43	Rooting: post dosing
		49	Rooting: post dosing
	163	24	Ataxia: post dosing
			Prone: post dosing
		25	Prone: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		32	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		42	Rooting: post dosing
		43	Rooting: post dosing
	180	24	Prone: post dosing
		25	Prone: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		42	Rooting: post dosing
		49	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 36 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
18	181	24	Prone: post dosing
		25	Prone: post dosing
		27	Rooting: post dosing
		28	Rooting: post dosing
		32	Salivation: prior to dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		38	Salivation: prior to dosing
			Rooting: post dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
			Rooting: post dosing
		41	Rooting: post dosing
		42	Rooting: post dosing
		48	Rooting: post dosing
		49	Rooting: post dosing
	190	23	Ataxia: post dosing
			Prone: post dosing
		24	Prone: post dosing
		26	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Rooting: post dosing
		41	Rooting: post dosing
	191	23	Ataxia: post dosing
			Prone: post dosing
		24	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rough coat
		34	Salivation: prior to dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 37 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
18	208	23	Prone: post dosing
		24	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		32	Rooting: post dosing
		47	Rooting: post dosing
	209	23	Ataxia: post dosing
			Prone: post dosing
		24	Prone: post dosing
		26	Salivation: prior to dosing
			Rooting: post dosing
		27	Salivation: prior to dosing
			Rooting: post dosing
		30	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		33	Rough coat
		34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Salivation: prior to dosing
		41	Salivation: prior to dosing
			Rooting: post dosing
		47	Rooting: post dosing
	226	23	Prone: post dosing
		24	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		31	Rooting: post dosing
		32	Rooting: post dosing
		34	Rooting: post dosing
		35	Rooting: post dosing
		36	Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		41	Rooting: post dosing
		47	Rooting: post dosing
		50	Salivation: prior to dosing
	227	23	Prone: post dosing
		24	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing

(continued)

Table A-8. Individual F_1 Male Clinical Observations During the Post Wean Period (page 38 of 38)

Group[a]	Animal ID	Postnatal Day	Clinical Observation
18	244	23	Prone: post dosing
		24	Prone: post dosing
		26	Rooting: post dosing
		27	Rooting: post dosing
		32	Rooting: post dosing
		37	Rooting: post dosing
	245	23	Prone: post dosing
		24	Prone: post dosing
		27	Salivation: prior to dosing
			Rooting: post dosing
		32	Salivation: prior to dosing
		33	Salivation: prior to dosing
			Rooting: post dosing
		34	Salivation: prior to dosing
			Rooting: post dosing
		35	Salivation: prior to dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Salivation: prior to dosing
			Rooting: post dosing
		40	Salivation: prior to dosing
		47	Rooting: post dosing
		48	Salivation: prior to dosing
	262	23	Prone: post dosing
		24	Efflux of the dosing solution
			Prone: post dosing
		30	Right front leg: bruised, animal not using it
		31	Right front leg: bruised, animal using it a little
		32	Right front leg: bruised, animal using it
			Rooting: post dosing
		37	Rooting: post dosing
		38	Rooting: post dosing
		39	Rooting: post dosing
		40	Right front paw: second digit missing
		41	Right front paw: second digit missing
			Rooting: post dosing
		42	Right front paw: second digit missing
		43	Right front paw: second digit missing

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.

Table A-9. Individual F_1 Male Preputial Separation Data (page 1 of 7)

Group[a]	Animal ID	Day of Acquisition[b]	Body Weight (g)
1	1	42	200.26
	15	40	190.40
	32	40	207.57
	33	43	223.55
	50	40	211.21
	51	48	270.36
	68	41	218.80
	69[c]		
	86[c]		
	87	40	233.18
	104	40	228.57
	105	39	209.51
	122	42	224.12
	123	42	216.45
	135[c]		
2	4	43	191.47
	18[d]		
	29	40	186.26
	36	44	230.61
	47	41	200.10
	54[e]		
	65	44	227.40
	72	44	233.59
	83	41	194.88
	90	40	187.78
	101	43	226.23
	108	44	229.11
	119[c]		
	126	39	188.24
	133	41	210.44
3	5	45	187.11
	13	45	201.64
	19	43	207.42
	28	42	194.88
	37	41	186.20
	46	43	199.71
	55[c]		
	64	44	216.04
	73	42	200.66
	82	42	204.39
	91	43	211.63
	100	43	201.52
	109	42	191.88
	118[c]		
	127[c]		

(continued)

Table A-9. Individual F_1 Male Preputial Separation Data (page 2 of 7)

Group[a]	Animal ID	Day of Acquisition[b]	Body Weight (g)
4	6	45	200.66
	12	45	217.86
	20[f]		
	27	46	268.08
	38	44	250.11
	45	46	258.99
	56	44	257.18
	63	46	267.67
	74[c]		
	81	46	271.26
	92	44	233.40
	99	46	282.29
	110	45	261.56
	117	44	239.12
	128	43	256.08
5	7	49	240.96
	21	47	290.53
	26	46	266.69
	39	46	255.84
	44	48	274.89
	57	45	250.55
	62	46	235.63
	75	45	244.02
	80	45	242.03
	93	44	242.29
	98	44	253.44
	111	46	276.10
	116	46	286.36
	129	45	275.09
	132	44	253.44
6	8	45	219.24
	11	45	224.36
	22	42	246.99
	25	44	214.62
	40	44	259.39
	43	44	227.08
	58	45	242.15
	61	44	258.84
	76	44	243.19
	79[c]		
	94	41	241.50
	97	44	248.84
	112	43	253.37
	115[c]		
	130	44	277.67

(continued)

Table A-9. Individual F_1 Male Preputial Separation Data (page 3 of 7)

Group[a]	Animal ID	Day of Acquisition[b]	Body Weight (g)
7	9[g]		
	10	47	248.92
	23	48	272.68
	24[c]		
	41	47	262.32
	42	48	261.29
	59[g]		
	60	48	276.21
	77	46	216.77
	78	46	248.04
	95	46	256.95
	96	45	269.64
	113	47	283.57
	114[c]		
	131[c]		
8	2	46	209.30
	16	42	232.09
	31	45	222.20
	34	40	200.07
	49	39	203.60
	52	39	217.60
	67	43	215.04
	70	43	238.84
	85	39	206.76
	88	40	205.17
	103	44	238.10
	106	45	254.26
	121	40	210.66
	124	40	208.17
	134[h]		
9	3	46	198.13
	14	42	179.13
	17[c]		
	30[c]		
	35	39	194.26
	48	42	223.16
	53	40	204.32
	66	42	225.20
	71	41	226.17
	84	45	247.42
	89	44	246.40
	102	41	230.30
	107	39	208.00
	120	42	256.74
	125	41	226.81

(continued)

Table A-9. Individual F_1 Male Preputial Separation Data (page 4 of 7)

Group[a]	Animal ID	Day of Acquisition[b]	Body Weight (g)
10	136	40	172.02
	153	42	208.83
	154	41	219.16
	171	41	212.35
	172	41	218.76
	182	40	239.12
	199	39	200.07
	200	38	203.97
	217[i]		
	218	39	193.38
	235	38	212.62
	236	40	219.50
	253	39	195.63
	254	38	198.93
	270	38	210.18
11	137	41	190.97
	152	41	212.28
	155	41	226.95
	170	39	202.83
	173	42	257.99
	183	40	190.97
	198	40	216.00
	201	41	223.34
	216	38	197.22
	219	41	217.60
	234	44	234.85
	237	40	219.40
	252	40	231.72
	255	38	200.66
	269	40	228.47
12	138	46	138.98
	151	46	136.24
	156	45	157.85
	169	45	176.96
	174	41	179.34
	184	44	153.07
	197	41	160.38
	202	41	157.54
	215	40	180.51
	220	44	174.85
	233	43	172.35
	238	41	173.38
	251	44	174.91
	256	44	188.63
	268	44	173.04

(continued)

Table A-9. Individual F_1 Male Preputial Separation Data (page 5 of 7)

Group[a]	Animal ID	Day of Acquisition[b]	Body Weight (g)
13	141	41	168.21
	148	40	211.06
	159	42	198.83
	166	41	218.10
	177	41	242.80
	187	41	210.83
	194	44	224.86
	205	44	250.26
	212	44	248.17
	223	44	243.74
	230	41	204.71
	241	44	267.87
	248	40	202.74
	259	44	251.63
	265	44	263.41
14	142	42	193.80
	147	45	223.03
	160	45	225.78
	165	45	224.36
	178	45	250.10
	188	44	224.64
	193	43	225.18
	206	44	238.71
	211	44	223.71
	224	45	231.79
	229	44	252.20
	242[j]		
	247	44	253.42
	260	44	260.22
	264	44	259.76
15	139	47	239.81
	150	45	224.48
	157	45	223.19
	168	45	238.29
	175	45	234.20
	185	44	228.34
	196	41	202.18
	203	44	234.03
	214	44	215.30
	221	44	240.11
	232	44	221.18
	239	44	241.03
	250	40	199.44
	257	41	236.33
	267	41	221.72

(continued)

Table A-9. Individual F_1 Male Preputial Separation Data (page 6 of 7)

Group[a]	Animal ID	Day of Acquisition[b]	Body Weight (g)
16	140	45	213.27
	149	47	200.89
	158	45	212.86
	167	47	204.56
	176	47	258.80
	186	45	226.83
	195	45	221.11
	204	44	191.41
	213	44	212.28
	222	44	214.36
	231	46	207.87
	240	46	246.64
	249	44	218.77
	258	44	244.77
	266	49	285.11
17	143	42	199.66
	146	41	206.12
	161	44	239.42
	164	42	245.79
	179	41	237.45
	189	40	203.76
	192	41	240.06
	207	40	205.58
	210	42	204.99
	225	44	262.46
	228	40	208.02
	243	40	232.75
	246	41	200.14
	261	40	203.99
	263	41	216.92
18	144	45	210.14
	145	41	205.42
	162	41	189.15
	163	45	253.89
	180	45	230.16
	181	45	213.77
	190	44	220.27
	191	44	218.26
	208	44	225.47
	209	40	219.27
	226	44	266.31
	227	40	219.84
	244	40	224.74
	245	43	238.94
	262	44	226.88

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.
[b]Postnatal day.
[c]Male was removed from the study because his correct postnatal day 0 could not be confirmed.
[d]Male was removed from the study because it was not dosed on the correct postnatal days.
[e]Male was found dead on postnatal day 37 after dosing (misdirected dose).
[f]Male was euthanized on postnatal day 29 after dosing due to a leg injury.
[g]Male was not positive for preputial separation by postnatal day 52 when it was necropsied and therefore it was excluded from the evaluation.
[h]Male was not positive for preputial separation by postnatal day 53 when it was necropsied and therefore it was excluded from the evaluation.
[i]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).
[j]Male was found dead on postnatal day 37 prior to dosing (misdirected dose).

Table A-9a. Summary and Statistical Analysis of the Preputial Separation Data for the Component 1 F_1 Males with the Data for Male 51 in the Control Group Removed (page 1 of 2)

	Atrazine (mg/kg/day, po)		p,p'DDE (mg/kg/day, po)[a]		Vinclozolin (mg/kg/day, po)		Methoxychlor (mg/kg/day, po)	
0	75	150	50	100	30	100	25	50
No. of Males on Study 12[b]	13[c]	12[d]	14[e]	15	13[f]	12[g]	15	13[h]
Number of Males Evaluated 12	12[i]	12	13[j]	15	13	10[k]	14[l]	13
Average Postnatal Day of Preputial Separation[m]								
40.8	42.0	42.9 Þ Þ Þ	44.9 ***	45.7 ***	43.8 ***	46.8 ***	41.8	41.8
± 0.4	± 0.5	± 0.4	± 0.3	± 0.4	± 0.3	± 0.3	± 0.7	± 0.6
N=11[n]	N=12	N=12	N=13	N=15	N=13	N=10	N=14	N=13
	# † † † Ÿ Ÿ Ÿ		‡ ‡ ‡ § § §		‡ ‡ ‡ § § §		#	
Average Body Weight (g) on Day of Acquisition[m]								
214.87	208.84	200.26 Þ Þ	251.10 ***	259.19 ***	242.86 ***	259.64 ***	218.70	220.46
± 3.83	± 5.57	± 2.64	± 6.35	± 4.58	± 4.97	± 5.98	± 4.33	± 6.32
N=11[n]	N=12	N=12	N=13	N=15	N=13	N=10	N=14	N=13
	# † † Ÿ Ÿ		‡ ‡ ‡ § § §		‡ ‡ ‡ § § §			

(continued)

Table A-9a. Summary and Statistical Analysis of the Preputial Separation Data for the Component 1 F_1 Males with the Data for Male 51 in the Control Group Removed (page 2 of 2)

[a] p,p'-Dichlorodiphenyldichloroethylene.
[b] Males 69, 86 and 135 were removed from the study because their correct postnatal day 0 could not be confirmed.
[c] Male 18 was removed from the study because it was not dosed on the correct postnatal days and male 119 was removed from the study because his correct postnatal day 0 could not be confirmed.
[d] Males 55, 118 and 127 were removed from the study because their correct postnatal day 0 could not be confirmed.
[e] Male 74 was removed from the study because his correct postnatal day 0 could not be confirmed.
[f] Males 79 and 115 were removed from the study because their correct postnatal day 0 could not be confirmed.
[g] Males 24, 114 and 131 were removed from the study because their correct postnatal day 0 could not be confirmed.
[h] Males 17 and 30 were removed from the study because their correct postnatal day 0 could not be confirmed.
[i] Male 54 was found dead on postnatal day 37 after dosing (misdirected dose).
[j] Male 20 was euthanized on postnatal day 29 after dosing due to a leg injury.
[k] Males 9 and 59 were not positive for preputial separation by postnatal day 52 when they were necropsied and therefore they were excluded from the evaluation.
[l] Male 134 was not positive for preputial separation by postnatal day 53 when it was necropsied and therefore it was excluded from the evaluation.
[m] Reported as the mean ± S.E.M.; pnd = postnatal day.
[n] Decrease in N is due to the study sponsor requesting that the data for male 51 be excluded.
[#] Levene's test for homogeneity of variances was significant ($p<0.05$), therefore robust regression methods were used to test all treatment effects.
[‡‡‡] $p<0.001$; ANOVA Test.
[§§§] $p<0.001$; Test for Linear Trend.
[***] $p<0.001$; Dunnett's Test.
[††] $p<0.01$; Wald Chi-square Test for overall treatment effect in robust regression model.
[†††] $p<0.001$; Wald Chi-square Test for overall treatment effect in robust regression model.
[ÿÿ] $p<0.01$; Linear trend test in robust regression model.
[ÿÿÿ] $p<0.001$; Linear trend test in robust regression model.
[þþ] $p<0.01$; Individual t-test for pairwise comparisons to control in robust regression model.
[þþþ] $p<0.001$; Individual t-test for pairwise comparisons to control in robust regression model.

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 1 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
1	1	.[c]	0.0102	0.0115	13.2886	0.0538	2.5402	2.4010	0.4574	0.2303	0.2066	0.4369	0.4206	0.5614	6.09	18.56
	15	289.77	0.0117	0.0198	14.7843	0.0495	2.8075	2.7284	0.4301	0.2036	0.1958	0.3994	0.5937	0.6477	5.79	11.71
	32	294.81	0.0102	0.0176	13.8965	0.0492	2.6208	2.8267	0.4519	0.1626	0.1773	0.3399	0.5705	0.6519	6.27	14.92
	33	300.84	0.0115	0.0139	14.0039	0.0612	2.7764	2.7839	0.4334	0.1988	0.1790	0.3778	0.4301	0.7037	6.27	11.12
	50	311.35	0.0117	0.0138	17.1200	0.0573	2.7948	2.9924	0.5224	0.2608	0.1313	0.3921	0.6732	0.8318	7.30	11.25
	51	302.98	0.0112	0.0210	18.6603	0.0391	2.8095	2.6171	0.4862	0.2772	0.1158	0.3930	0.6820	0.6714	6.88	9.45
	68	321.67	0.0102	0.0243	14.7715	0.0554	2.8144	2.7562	0.4383	0.2807	0.1697	0.4504	0.6095	0.9028	5.95	6.71
	69	.[d]														
	86	.[d]														
	87	355.20	0.0139	0.0178	17.6223	0.0588	3.4601	2.6754	0.5021	0.2563	0.3053	0.5616	0.7511	0.7117	5.69	7.75
	104	343.86	0.0111	0.0218	20.0416	0.0611	3.4086	3.0541	0.5767	0.2216	0.1853	0.4069	0.4256	0.6489	7.41	7.33
	105	340.34	0.0111	0.0223	18.8908	0.0459	2.8508	2.7476	0.4944	0.2950	0.3032	0.5982	0.4781	0.7428	6.36	15.13
	122	311.36	0.0113	0.0225	17.0049	0.0678	2.4754	2.6888	0.5108	0.2352	0.1762	0.4114	0.4282	0.7227	6.90	9.86
	123	307.19	0.0120	0.0153	16.8751	0.0418	2.8699	2.6113	0.5240	0.2660	0.2224	0.4884	0.5722	0.6752	6.64	7.62
	135	.[d]														
2	4	246.75	0.0091	0.0224	13.4750	0.0400	2.5788	2.4279	0.3558	0.1532	0.1458	0.2990	0.3297	0.3526	7.54	8.63
	18	.[e]														
	29	275.50	0.0127	0.0209	13.1050	0.0481	2.4360	2.8329	0.3867	0.1767	0.1706	0.3473	0.5305	0.5968	7.26	19.63
	36	297.47	0.0116	0.0191	14.7592	0.0536	2.6566	2.7253	0.4693	0.2131	0.1590	0.3721	0.3847	0.7131	5.65	12.67
	47	263.90	0.0094	0.0219	13.4581	0.0532	2.5396	2.8331	0.4747	0.2329	0.2360	0.4689	0.5906	0.8472	5.52	16.71
	54	.[f]														
	65	287.61	0.0102	0.0242	15.9369	0.0506	2.5868	2.8153	0.4075	0.2084	0.1805	0.3889	0.5451	0.6475	6.34	6.67
	72	298.69	0.0120	0.0187	15.6290	0.0383	3.1124	3.1209	0.4668	0.3113	0.2019	0.5132	0.5821	0.6560	6.50	6.89
	83	264.16	0.0106	0.0255	13.4238	0.0510	2.7684	3.0027	0.5305	0.1568	0.1691	0.3259	0.4191	0.5138	6.51	6.96
	90	284.01	0.0087	0.0180	15.2215	0.0464	2.6899	2.9504	0.4517	0.1344	0.1695	0.3039	0.4185	0.5753	4.72	14.53
	101	294.42	0.0103	0.0181	16.3522	0.0489	2.9086	2.5369	0.4712	0.1992	0.1704	0.3696	0.3838	0.4103	5.65	7.41
	108	279.41	0.0078	0.0176	15.7600	0.0612	2.7247	2.7093	0.4710	0.2322	0.2252	0.4574	0.3473	0.7609	6.90	13.42
	119	.[d]														
	126	269.99	0.0078	0.0181	16.0756	0.0583	2.8921	2.8152	0.4452	0.2239	0.1640	0.3879	0.4331	0.5381	7.77	5.83
	133	286.05	0.0096	0.0215	14.9008	0.0462	2.7829	3.0393	0.4434	0.2684	0.1629	0.4313	0.4694	0.5414	5.89	11.32

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 2 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
3	5	230.92	0.0071	0.0230	13.3966	0.0467	2.3889	2.1992	0.3156	0.2326	0.1389	0.3715	0.3886	0.4692	7.99	10.61
	13	250.22	0.0036	0.0184	14.3621	0.0467	2.4823	2.6660	0.4042	0.2058	0.1556	0.3614	0.3275	0.4056	6.72	9.27
	19	267.23	0.0100	0.0159	14.3547	0.0552	2.5810	2.9241	0.3970	0.1580	0.2223	0.3803	0.4078	0.5477	6.19	27.97
	28	257.00	0.0082	0.0178	13.5722	0.0584	2.6858	2.7516	0.4228	0.1582	0.1354	0.2936	0.3726	0.6273	6.60	16.25
	37	248.51	0.0087	0.0178	12.8434	0.0534	2.3125	2.7959	0.4353	0.2410	0.1591	0.4001	0.3212	0.3850	7.23	8.50
	46	255.04	0.0072	0.0236	14.1255	0.0633	2.4419	2.7616	0.4843	0.1133	0.1091	0.2224	0.4969	0.5151	5.85	8.09
	55	.[d]														
	64	255.74	0.0075	0.0173	13.6510	0.0446	2.5329	2.9607	0.4254	0.2340	0.2107	0.4447	0.4663	0.7752	5.64	7.97
	73	259.71	0.0087	0.0193	13.6200	0.0460	2.6055	3.0264	0.4829	0.2097	0.1683	0.3780	0.4128	0.7342	6.31	13.43
	82	267.31	0.0085	0.0170	13.7582	0.0578	2.4473	2.9128	0.4007	0.1648	0.1358	0.3006	0.3727	0.5500	5.57	21.33
	91	289.66	0.0094	0.0176	16.4653	0.0672	2.9448	3.0848	0.4233	0.1622	0.1266	0.2888	0.5851	0.6060	4.99	10.63
	100	261.37	0.0074	0.0186	14.9350	0.0524	2.7134	2.9302	0.4449	0.2505	0.1781	0.4286	0.4353	0.5537	5.29	9.16
	109	237.27	0.0090	0.0173	12.3738	0.0533	2.3170	2.8222	0.4120	0.2321	0.1323	0.3644	0.4584	0.5523	7.01	8.65
	118	.[d]														
	127	.[d]														
4	6	255.04	0.0107	0.0209	20.1726	0.0508	2.8882	2.5374	0.4216	0.1821	0.1801	0.3622	0.4319	0.4588	5.18	14.99
	12	274.09	0.0101	0.0196	20.9250	0.0475	2.8140	2.6557	0.4294	0.1723	0.1531	0.3254	0.4519	0.4523	6.35	10.50
	20	.[g]														
	27	323.19	0.0097	0.0209	21.9346	0.0496	3.0406	2.7345	0.3785	0.1568	0.2149	0.3717	0.4612	0.5158	6.13	9.16
	38	319.03	0.0095	0.0237	21.9889	0.0465	3.3214	3.0784	0.4845	0.2323	0.1880	0.4203	0.6039	0.8856	6.59	25.32
	45	318.44	0.0105	0.0187	22.4093	0.0581	3.4293	3.0349	0.4831	0.3444	0.1933	0.5377	0.7772	0.8005	6.27	24.92
	56	342.49	0.0116	0.0218	23.9160	0.0648	3.0641	3.0415	0.4880	0.2905	0.1874	0.4779	0.5107	0.7751	6.64	14.30
	63	313.76	0.0128	0.0192	20.0843	0.0628	3.0843	2.6534	0.5520	0.2949	0.2521	0.5470	0.5965	0.6700	5.30	8.67
	74	.[d]														
	81	333.65	0.0109	0.0240	25.8598	0.0595	3.4473	2.7541	0.5227	0.2444	0.2692	0.5136	0.6546	0.6861	6.58	12.01
	92	305.48	0.0071	0.0199	20.0806	.[h]	2.9070	2.8503	0.4889	0.2022	0.2035	0.4057	0.6160	0.6252	5.68	17.52
	99	347.60	0.0140	0.0217	25.4090	0.0509	3.7538	2.6574	0.3923	0.2629	0.2402	0.5031	0.5238	0.6867	6.60	9.44
	110	319.19	0.0121	0.0254	19.9780	0.0501	3.0347	2.8293	0.4882	0.2478	0.2085	0.4563	0.5822	0.7489	4.98	12.15
	117	320.80	0.0103	0.0267	26.1122	0.0395	3.2171	2.7877	0.4433	0.3326	0.2478	0.5804	0.5365	0.6110	6.47	8.14
	128	345.70	0.0143	0.0232	23.4821	0.0634	3.4981	2.7339	0.4984	0.3862	0.3164	0.7026	0.5957	0.9416	3.88	15.60

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 3 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
5	7	218.95	.[h]	0.0132	14.7831	0.0583	2.0625	2.3136	0.3239	0.2342	0.1796	0.4138	0.2886	0.5138	3.75	6.48
	21	320.22	0.0114	0.0255	26.4993	0.0501	3.3607	2.4766	0.3901	0.1618	0.2086	0.3704	0.4125	0.6091	5.27	13.82
	26	328.65	0.0124	0.0145	24.2421	0.0713	3.4392	2.7868	0.3808	0.3184	0.1372	0.4556	0.4605	0.5931	6.90	13.53
	39	298.02	0.0114	0.0245	23.2136	0.0594	3.1548	2.6881	0.4337	0.2240	0.1584	0.3824	0.2098	0.4401	5.32	14.65
	44	311.50	0.0112	0.0170	20.6537	0.0633	2.9875	2.8081	0.4854	0.2402	0.1376	0.3778	0.3695	0.4584	6.86	15.20
	57	309.89	0.0147	0.0315	24.5415	0.0453	3.1702	3.0830	0.4650	0.2190	0.1224	0.3414	0.4491	0.8193	5.98	21.79
	62	281.55	0.0107	0.0246	23.2149	0.0380	3.1690	2.6809	0.4725	0.1985	0.0467	0.2452	0.6203	0.6419	4.17	15.23
	75	295.78	0.0102	0.0249	25.5471	0.0186	3.2511	2.5508	0.4318	0.0831	0.2976	0.3807	0.5379	0.6076	6.56	8.39
	80	312.51	0.0125	0.0304	22.6323	0.0442	3.0889	2.6529	0.3576	0.1734	0.2205	0.3939	0.5794	0.6834	5.35	34.68
	93	323.58	0.0111	0.0274	26.3418	0.0427	2.9567	2.8469	0.4473	0.2042	0.2510	0.4552	0.5449	0.5703	4.96	8.34
	98	321.77	0.0122	0.0228	24.1526	0.0584	3.1349	2.9790	0.5432	0.2888	0.2735	0.5623	0.4352	0.6590	4.54	9.67
	111	330.76	0.0090	0.0355	24.1677	0.0450	3.3675	2.8374	0.4228	0.2607	0.1735	0.4342	0.5082	0.6386	5.54	12.40
	116	339.64	0.0116	0.0218	27.1037	0.0606	3.9099	3.0402	0.4818	0.2534	0.2091	0.4625	0.7258	0.6481	5.70	19.24
	129	343.25	0.0129	0.0291	25.9342	0.0555	3.4942	2.7180	0.4309	0.3255	0.2998	0.6253	0.5906	0.5856	4.95	8.53
	132	330.30	0.0115	0.0221	24.1322	0.0544	3.4903	3.1778	0.4667	0.2429	0.2152	0.4581	0.6042	0.8572	3.92	14.42
6	8	282.43	0.0128	0.0218	16.4681	0.0522	2.8500	2.6754	0.3689	0.1748	0.1300	0.3048	0.4470	0.4895	5.54	11.54
	11	279.78	0.0107	0.0215	15.7760	0.0544	2.6022	2.7085	0.4174	0.2656	0.2289	0.4945	0.4204	0.4991	6.52	11.86
	22	364.66	0.0143	0.0212	22.2210	0.0568	3.1328	2.6812	0.4634	0.4052	0.2783	0.6835	0.5759	0.6121	5.31	8.85
	25	286.90	0.0107	0.0190	12.9937	0.0486	2.5335	2.8351	0.3679	0.2155	0.2043	0.4198	0.4101	0.5531	3.63	5.85
	40	334.03	0.0113	0.0196	19.2067	0.0680	2.7023	2.9267	0.4546	0.2764	0.1402	0.4166	0.2338	0.5934	4.80	8.78
	43	284.97	0.0096	0.0177	12.7340	0.0530	2.4074	2.7798	0.4037	0.2543	0.1202	0.3745	0.5388	0.8911	5.38	9.87
	58	300.04	0.0105	0.0227	16.3954	0.0592	2.9989	3.0752	0.4716	0.1880	0.2263	0.4143	0.3278	0.7213	4.84	9.98
	61	323.66	0.0112	0.0169	18.4137	0.0568	3.0956	3.0001	0.5004	0.2399	0.1282	0.3681	0.2979	0.7703	4.91	12.08
	76	314.65	0.0113	0.0228	20.2619	0.0554	3.2945	3.0021	0.5016	0.2362	0.2326	0.4688	0.4579	0.6830	3.59	10.53
	79	.[d]														
	94	356.65	0.0094	0.0160	20.0673	0.0709	3.1400	3.1598	0.4701	0.2470	0.1963	0.4433	0.4858	0.5777	3.80	14.14
	97	338.81	0.0113	0.0157	18.3495	0.0486	3.0026	2.9375	0.5097	0.3024	0.1753	0.4777	0.5861	0.8192	4.32	12.18
	112	343.66	0.0129	0.0226	18.0244	0.0560	3.2632	3.5780	0.5277	0.3261	0.1918	0.5179	0.6301	1.0304	5.23	8.55
	115	.[d]														
	130	364.84	0.0122	0.0195	19.0774	0.0702	3.8339	3.1272	0.4725	0.2255	0.2269	0.4524	0.6397	0.6741	5.40	13.23

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 4 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
7	9	276.51	0.0098	0.0187	14.6754	0.0455	2.5529	2.4298	0.3547	0.2291	0.0977	0.3268	0.2740	0.5238	6.20	20.49
	10	288.68	0.0116	0.0234	16.6082	0.0476	2.6018	2.5511	0.3279	0.1919	0.1240	0.3159	0.3243	0.4530	5.03	11.12
	23	307.67	0.0112	0.0194	16.6452	0.0459	2.7785	2.8337	0.3582	0.1617	0.1598	0.3215	0.2897	0.5218	4.16	12.03
	24	.[d]														
	41	298.31	0.0127	0.0184	17.7970	0.0686	2.8362	3.0495	0.4283	0.2091	0.1770	0.3861	0.1879	0.4556	4.55	16.47
	42	292.89	0.0104	0.0187	15.4234	0.0458	2.5784	3.1554	0.4007	0.2854	0.1271	0.4125	0.3449	0.5648	4.59	7.80
	59	293.84	0.0116	0.0191	16.1725	0.0748	2.8525	3.0597	0.3663	0.1726	0.1305	0.3031	0.1670	0.4256	4.17	10.13
	60	315.86	0.0092	0.0187	21.6926	.[h]	2.9851	2.9918	0.4725	0.2129	0.0517	0.2646	0.3494	0.7211	4.54	8.58
	77	286.89	0.0105	0.0253	15.6958	0.0552	2.6850	2.8882	0.4104	0.1812	0.1224	0.3036	0.3403	0.4440	3.70	14.26
	78	310.52	0.0133	0.0222	14.9983	0.0548	2.7221	3.0836	0.4188	0.1476	0.1061	0.2537	0.3436	0.5234	3.62	13.11
	95	309.28	0.0090	0.0196	17.1613	0.0524	3.1049	2.6961	0.3724	0.2231	0.1614	0.3845	0.2973	0.6544	4.03	8.01
	96	345.93	0.0118	0.0212	20.3813	0.0840	3.2289	3.1023	0.5191	0.1975	0.1724	0.3699	0.4136	0.6032	3.81	14.92
	113	.[c]	0.0089	0.0213	20.4721	0.0549	2.7435	3.3767	0.3720	0.2650	0.1271	0.3921	0.3205	0.6403	3.01	17.43
	114	.[d]														
	131	.[d]														
8	2	249.62	0.0106	0.0163	11.5504	0.0485	1.8262	2.2830	0.4201	0.1551	0.1208	0.2759	0.3819	0.4816	5.73	22.15
	16	316.99	0.0123	0.0231	16.2780	0.0470	2.7041	2.6073	0.4153	0.1369	0.1298	0.2667	0.4504	0.6238	6.91	12.25
	31	290.35	0.0113	0.0183	13.7935	0.0444	2.7131	2.8704	0.5113	0.2112	0.1638	0.3750	0.5024	0.7980	7.08	11.41
	34	295.50	0.0114	0.0177	13.9106	.[i]	2.6817	2.8405	0.4663	0.1832	0.1868	0.3700	0.5428	0.5494	6.25	14.91
	49	302.08	0.0118	0.0230	14.5328	0.0592	3.1307	2.7539	0.5393	0.2512	0.1664	0.4176	0.6575	0.6769	6.82	11.51
	52	321.72	0.0077	0.0196	17.7581	.[h]	2.9748	2.9260	0.5437	0.2660	0.1412	0.4072	0.6642	0.7733	5.88	27.93
	67	267.23	0.0095	0.0194	13.0736	0.0572	2.5671	2.7283	0.5182	0.2446	0.1793	0.4239	0.3404	0.4858	6.19	8.13
	70	314.21	0.0115	0.0276	17.4700	0.0647	3.4145	2.8813	0.4640	0.2502	0.1214	0.3716	0.5384	0.7843	6.99	6.32
	85	327.87	0.0120	0.0167	17.3200	0.0648	2.9511	2.8848	0.5133	0.2451	0.1658	0.4109	0.5152	0.6621	6.60	7.60
	88	297.04	0.0106	0.0213	13.8654	0.0501	2.4354	2.6506	0.4230	0.2017	0.1708	0.3725	0.4181	0.5797	7.37	8.08
	103	311.16	0.0107	0.0221	16.7954	0.0560	2.2682	2.6103	0.5530	0.3667	0.2479	0.6146	.[j]	0.7125	6.24	7.01
	106	301.47	0.0077	0.0230	13.9063	0.0539	2.7307	2.7370	0.4956	0.2740	0.1049	0.3789	0.4677	0.7879	5.60	6.72
	121	321.29	0.0125	0.0221	17.5331	0.0609	3.1978	3.3115	0.5450	0.2423	0.2071	0.4494	0.5246	0.9893	4.32	5.44
	124	296.88	0.0114	0.0282	16.9468	0.0769	2.9474	2.8223	0.4667	0.2700	0.2606	0.5306	0.4894	0.5105	5.49	8.90
	134	316.18	0.0120	0.0170	16.5189	0.0655	3.1334	2.6528	0.5248	0.2676	0.2161	0.4837	0.5252	0.8450	4.22	6.40

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 5 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
9	3	238.34	0.0103	0.0120	10.7471	0.0499	2.0486	2.1970	0.3572	0.1615	0.1240	0.2855	0.2538	.[k]	5.58	10.10
	14	248.60	0.0112	0.0139	12.7138	0.0463	2.4471	2.5543	0.3773	0.1563	0.1238	0.2801	0.4307	0.4612	7.13	11.21
	17	.[d]														
	30	.[d]														
	35	296.39	0.0107	0.0170	14.3110	0.0669	2.7639	3.0660	0.4339	0.2101	0.1872	0.3973	0.3293	0.5598	5.86	13.21
	48	290.45	.[h]	0.0172	15.1739	0.0679	2.9837	2.6561	0.4899	0.2327	0.0761	0.3088	0.3184	0.4348	7.17	9.92
	53	294.82	0.0096	0.0124	14.9200	0.0560	2.8656	2.8866	0.4790	0.3274	0.1803	0.5077	0.2409	0.6770	6.92	10.85
	66	297.38	0.0123	0.0154	14.9000	0.0516	3.0540	2.6535	0.4370	0.3030	0.1567	0.4597	0.5032	0.8630	5.46	8.62
	71	297.45	0.0092	0.0166	14.6546	0.0607	2.8959	2.6802	0.5067	0.2527	0.1958	0.4485	0.4385	0.5128	6.83	11.35
	84	300.39	0.0087	0.0150	14.8100	0.0765	2.3291	2.3780	0.4126	0.2429	0.1854	0.4283	0.3654	0.5329	7.26	13.55
	89	306.70	0.0103	0.0232	16.1744	0.0642	2.5820	2.8520	0.5613	0.2650	0.2152	0.4802	0.4293	0.5725	8.10	10.07
	102	331.45	0.0124	0.0190	17.5206	0.0731	3.5649	2.9401	0.4817	0.3186	0.1897	0.5083	0.7663	0.7445	7.58	7.49
	107	310.65	0.0109	0.0197	17.0916	0.0811	3.2342	3.1744	0.5435	0.2622	0.2084	0.4706	0.4793	0.5869	7.32	10.64
	120	352.75	0.0101	0.0189	17.9763	.[i]	3.0133	2.8643	0.4776	0.2085	0.2068	0.4153	0.3511	0.6128	5.42	17.05
	125	304.15	0.0118	0.0187	15.9546	0.0817	2.9351	2.8912	0.5125	0.2202	0.1855	0.4057	0.3494	0.7563	5.97	6.90
10	136	268.43	0.0107	0.0215	15.2893	0.0430	2.6217	2.7582	0.3986	0.1648	0.1906	0.3554	0.5333	0.4819	5.68	9.66
	153	299.89	0.0104	0.0335	15.6513	0.0460	3.0356	2.8389	0.4221	0.2276	0.1245	0.3521	0.6563	0.5056	7.89	13.45
	154	323.42	0.0101	0.0257	17.3441	0.0606	3.0151	2.9145	0.4233	0.2765	0.1636	0.4401	0.6422	0.5711	6.80	10.55
	171	316.44	0.0109	0.0242	17.9430	0.0473	2.8261	2.7569	0.4200	0.2606	0.1646	0.4252	.[j]	0.5749	6.09	7.92
	172	308.18	0.0073	0.0297	15.8077	0.0504	3.2064	2.8078	0.3990	0.2297	0.1298	0.3595	0.5305	0.5521	6.73	7.03
	182	373.28	0.0132	0.0339	23.9654	0.0462	3.8580	3.0265	0.5179	0.2345	0.2445	0.4790	0.8294	0.7450	5.51	11.90
	199	320.07	0.0130	0.0264	17.2041	0.0460	3.3432	2.7246	0.5315	0.1636	0.1248	0.2884	0.5526	0.7710	4.67	12.89
	200	334.72	0.0123	0.0247	17.8729	0.0457	3.3308	2.8490	0.4754	0.2739	0.2257	0.4996	0.4834	0.6448	5.93	10.72
	217	.[l]														
	218	293.28	0.0110	0.0338	16.7044	0.0459	2.9051	2.9551	0.4506	0.3341	0.2355	0.5696	0.5100	0.6788	4.57	7.57
	235	339.88	0.0132	0.0269	17.7423	0.0479	3.3063	2.9322	0.4252	0.3924	0.1919	0.5843	0.8445	0.7672	4.29	9.65
	236	329.09	0.0127	0.0266	18.2380	0.0511	3.1269	2.8797	0.4766	0.2922	0.2046	0.4968	0.8253	0.7634	4.45	20.07
	253	310.97	0.0110	0.0285	16.1014	0.0505	2.9009	3.1066	0.5671	0.3322	0.2800	0.6122	0.4582	0.6664	6.12	12.95
	254	326.23	0.0169	0.0215	17.1801	0.0559	2.9385	2.7379	0.4779	0.2507	0.1379	0.3886	0.9490	0.7031	6.14	14.01
	270	345.87	0.0105	0.0254	19.6305	0.0349	3.1905	2.8616	0.4042	0.2875	0.1749	0.4624	0.5005	0.5125	6.07	13.12

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 6 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
11	137	233.90	0.0120	0.0697	11.0393	0.0275	1.8680	2.6308	0.2898	0.1774	0.1961	0.3735	0.4110	0.5617	.[m]	111.64
	152	286.22	0.0131	0.0593	13.6800	0.0443	2.1539	2.6230	0.3766	0.2428	0.1657	0.4085	0.6138	0.5689	0.34	60.43
	155	284.64	0.0116	0.0489	14.4095	0.0336	2.3819	2.6660	0.3887	0.2023	0.1597	0.3620	0.4839	0.5934	.[m]	92.25
	170	276.66	0.0116	0.0961	13.2111	0.0378	2.4590	2.8952	0.4034	0.2183	0.1839	0.4022	0.6410	0.5943	0.50	71.98
	173	345.04	0.0115	0.1082	18.4648	0.0430	2.7076	2.9261	0.4525	0.3249	0.2606	0.5855	0.7725	0.6680	1.06	55.86
	183	291.65	0.0083	0.0774	15.2806	0.0422	2.5439	2.9280	0.4841	0.2518	0.1077	0.3595	0.7525	0.9834	0.52	83.31
	198	311.13	0.0108	0.0947	15.4070	0.0413	2.5878	2.6507	0.4429	0.2075	0.1199	0.3274	0.7237	0.5446	.[m]	64.26
	201	297.92	0.0117	0.0831	14.9490	0.0356	3.0038	2.8033	0.5072	0.2865	0.2339	0.5204	0.6601	0.7380	.[m]	83.76
	216	325.70	0.0119	0.1003	19.6343	0.0452	2.9837	2.5508	0.4213	0.1811	0.1599	0.3410	0.9681	0.7408	0.67	57.72
	219	255.98	0.0116	0.0597	10.9364	0.0348	2.0614	2.8392	0.3987	0.1874	0.1173	0.3047	0.6144	0.5324	0.38	91.48
	234	299.54	0.0114	0.0820	16.2718	0.0444	2.4796	3.0582	0.4826	0.2397	0.2003	0.4400	0.4375	0.5910	.[m]	77.95
	237	287.25	0.0119	0.0697	16.7200	0.0350	2.5874	2.7908	0.4889	0.2124	0.1121	0.3245	0.7227	0.5763	0.34	108.04
	252	296.39	.[h]	0.0714	15.0702	0.0347	2.3820	3.0835	0.4760	0.2166	0.1519	0.3685	0.9560	0.5838	0.42	102.04
	255	288.51	0.0127	0.0674	14.3812	0.0350	2.1144	2.9722	0.4320	0.2861	0.2353	0.5214	0.8465	0.6952	.[m]	92.07
	269	330.03	0.0129	0.0671	18.8092	0.0432	2.8390	2.6039	0.5342	0.3796	0.1330	0.5126	0.7616	0.8364	0.50	79.12
12	138	.[n]	0.0082	0.1316	6.6111	0.0278	1.1421	2.2432	0.3447	0.1743	0.1103	0.2846	0.2091	0.3249	.[m]	61.44
	151	139.78	0.0072	0.0484	5.4073	0.0232	1.1506	2.5026	0.3054	0.1072	0.0639	0.1711	0.3950	0.2385	.[m]	117.78
	156	162.05	0.0102	0.0760	6.4584	0.0210	1.3181	2.6500	0.3501	0.2057	0.1185	0.3242	0.5886	0.3297	.[m]	133.31
	169	178.36	0.0105	0.1511	7.6015	0.0311	1.3356	2.7359	0.3412	0.1463	0.1502	0.2965	0.4691	0.3072	0.33	128.91
	174	175.63	0.0107	0.0723	6.4552	0.0314	1.3778	2.9400	0.4246	0.1929	0.1006	0.2935	0.4843	0.3529	0.38	161.75
	184	157.46	0.0089	0.0885	7.3402	0.0230	1.4106	2.4126	0.3025	0.1310	0.1035	0.2345	0.5307	0.2823	.[m]	113.40
	197	175.07	0.0089	0.0959	8.5362	0.0240	1.5312	2.6979	0.4466	0.3006	0.0649	0.3655	0.6943	0.6849	.[m]	125.53
	202	166.32	0.0082	0.0796	7.1411	0.0245	1.5318	2.6613	0.3851	0.1779	0.1719	0.3498	0.6053	0.3099	.[m]	173.42
	215	190.83	0.0090	0.0817	9.5966	0.0313	1.6059	2.9126	0.4554	0.3014	0.1511	0.4525	0.3809	0.4185	.[m]	155.11
	220	179.65	0.0098	0.0896	8.4431	0.0304	1.5608	2.5119	0.4420	0.2337	0.2038	0.4375	0.6627	0.5001	0.41	151.06
	233	178.52	0.0146	0.0786	8.4094	0.0217	1.3674	2.4587	0.3911	0.1819	0.1623	0.3442	0.5302	0.2810	.[m]	143.44
	238	185.84	0.0090	0.0791	8.4734	0.0211	1.4182	2.7717	0.4111	0.1189	0.1223	0.2412	0.7354	0.4512	0.36	107.24
	251	182.42	0.0085	0.0848	7.7825	0.0245	1.5429	2.7335	0.3736	0.1737	0.1245	0.2982	0.4694	0.3890	0.36	141.69
	256	188.92	0.0113	0.0831	9.5444	0.0212	1.6238	2.8623	0.3340	0.1983	0.1867	0.3850	0.5870	0.3124	0.40	170.73
	268	.[o]														

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 7 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
13	141	265.43	0.0085	0.0206	15.2718	0.0523	2.6358	2.6178	0.3818	0.1824	0.1183	0.3007	0.4915	0.5835	5.53	6.75
	148	320.05	0.0116	0.0261	19.8011	0.0613	3.2611	2.9561	0.4098	0.2847	0.1393	0.4240	0.5170	0.6287	5.61	14.18
	159	282.82	0.0102	0.0278	17.3819	0.0435	2.7373	2.7048	0.3149	0.2425	0.1655	0.4080	0.3664	0.5081	6.24	7.43
	166	310.07	0.0114	0.0234	17.6193	0.0836	2.9049	2.9963	0.4414	0.1931	0.0796	0.2727	0.5111	0.3560	5.15	13.48
	177	347.18	0.0102	0.0192	20.7444	0.0785	3.2210	3.1680	0.4317	0.1976	0.0817	0.2793	0.5409	0.5558	5.31	10.47
	187	301.81	0.0109	0.0247	16.6796	0.0661	3.0240	3.0187	0.3842	0.2401	0.1244	0.3645	0.4503	0.6340	5.17	10.69
	194	287.93	0.0115	0.0298	15.7052	0.0543	2.6834	2.5441	0.4123	0.2158	0.1364	0.3522	0.4269	0.4804	4.89	8.60
	205	328.08	0.0090	0.0318	21.3076	0.0747	3.0509	2.4632	0.4403	0.1910	0.1570	0.3480	0.4054	0.7173	4.02	7.31
	212	323.32	0.0138	0.0281	20.0329	0.0879	3.0942	2.9565	0.4101	0.2966	0.1769	0.4735	0.4646	0.5682	6.75	9.63
	223	314.23	0.0115	0.0327	19.5372	0.0852	3.3423	2.8108	0.4426	0.1728	0.1142	0.2870	0.4657	0.4277	5.76	7.24
	230	304.78	0.0090	0.0301	20.5532	0.0720	3.2662	3.0906	0.5293	0.3007	0.2768	0.5775	0.5598	0.6337	5.48	8.30
	241	355.54	0.0109	0.0278	20.3301	0.0889	3.3114	2.7684	0.5202	0.3077	0.2112	0.5189	0.3921	0.5584	6.09	9.55
	248	326.86	0.0116	0.0195	21.1596	0.0731	3.2142	2.5377	0.4043	0.2461	0.1727	0.4188	0.6243	0.5940	4.77	10.68
	259	314.11	0.0089	0.0303	21.5657	0.0747	3.1372	2.6603	0.4353	0.2518	0.1574	0.4092	0.6130	0.7204	7.30	13.09
	265	353.06	0.0113	0.0264	20.2411	0.0599	3.6472	2.7836	0.4835	0.2350	0.2469	0.4819	0.3547	0.6699	5.56	12.96
14	142	261.19	0.0097	0.0265	15.5572	0.0619	2.5635	2.5962	0.3990	0.0589	0.1286	0.1875	0.2932	0.4956	6.23	11.54
	147	276.11	0.0107	0.0239	16.8246	0.0860	2.7581	2.7823	0.3983	0.2140	0.1259	0.3399	0.3268	0.4761	5.83	11.24
	160	276.03	0.0100	0.0288	16.5424	0.0790	2.5782	2.6642	0.3476	0.1233	0.0686	0.1919	0.3116	0.4002	5.70	10.31
	165	273.75	0.0102	0.0279	16.8484	0.0738	2.6895	2.8157	0.4230	0.2334	0.1503	0.3837	0.4540	0.4975	6.92	9.76
	178	309.03	0.0097	0.0244	17.7653	0.1075	3.2857	2.8237	0.3712	0.2020	0.1020	0.3040	0.4583	0.4160	5.33	8.49
	188	288.14	0.0142	0.0235	17.1234	0.1131	3.6148	2.7062	0.4322	0.3413	0.1365	0.4778	0.5426	0.7763	6.10	8.89
	193	296.85	0.0140	0.0278	18.7725	0.1084	3.8480	2.7640	0.4613	0.3380	0.1887	0.5267	0.7379	0.7512	5.36	8.69
	206	301.20	0.0116	0.0270	18.1900	0.1141	3.1269	2.7645	0.3542	0.0897	0.0740	0.1637	0.4181	0.4337	5.25	15.64
	211	290.34	0.0117	0.0263	18.1705	0.0724	2.8332	2.5560	0.4017	0.1593	0.1841	0.3434	0.2658	0.4942	5.32	9.43
	224	287.98	0.0091	0.0227	17.8265	0.0812	2.8541	2.7954	0.4494	0.3022	0.2393	0.5415	0.2266	0.5684	4.25	19.48
	229	337.76	0.0138	0.0291	23.8740	0.0824	3.4362	2.7373	0.4261	0.0983	0.1750	0.2733	0.5398	0.5715	4.32	11.52
	242	.[p]														
	247	335.92	0.0147	0.0289	24.0545	0.1104	3.6851	2.7310	0.4978	0.2019	0.1788	0.3807	0.5506	0.5461	5.94	14.33
	260	345.72	0.0114	0.0306	23.0081	0.0998	3.5310	2.7431	0.4015	0.2523	0.1382	0.3905	0.3756	0.5203	6.27	8.32
	264	341.02	0.0132	0.0270	23.4041	0.0815	3.4309	2.6171	0.4018	0.2672	0.1757	0.4429	0.3693	0.6476	6.34	8.39

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 8 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
15	139	275.54	0.0099	0.0289	16.1382	0.0430	2.6605	2.5875	0.3176	0.1937	0.0714	0.2651	0.2377	0.3136	4.69	10.77
	150	278.12	0.0092	0.0298	14.8480	0.0510	2.8287	2.6633	0.4269	0.1581	0.1867	0.3448	0.4718	0.4634	4.84	9.64
	157	272.77	0.0098	0.0234	13.5665	0.0491	2.5701	2.8482	0.3941	0.1793	0.1005	0.2798	0.3912	0.4360	4.70	10.40
	168	290.77	0.0075	0.0289	14.6707	0.0526	2.8529	2.9119	0.3942	0.1933	0.1193	0.3126	0.4706	0.4360	5.23	8.11
	175	293.71	0.0067	0.0367	15.2936	0.0478	3.2323	3.0946	0.3248	0.1825	0.1131	0.2956	0.3476	0.4266	7.48	8.19
	185	290.21	0.0099	0.0283	15.9456	0.0555	2.8810	2.9281	0.4741	0.2662	0.1365	0.4027	0.4701	0.5060	4.73	5.92
	196	304.09	0.0118	0.0352	16.4432	0.0580	3.1694	2.7290	0.4584	.[h]	0.2385	.[q]	0.2301	0.7321	4.30	12.05
	203	302.45	0.0114	0.0296	19.3331	0.0529	3.2074	2.8674	0.4311	0.1826	0.1765	0.3591	0.6403	0.5591	3.65	11.85
	214	271.87	0.0099	0.0335	15.4315	0.0354	2.7740	2.5462	0.3888	0.1587	0.1518	0.3105	0.5490	0.5239	.[r]	.[r]
	221	303.05	0.0084	0.0249	17.9891	0.0535	2.9334	2.4024	0.4149	0.1745	0.1852	0.3597	0.3787	0.6710	3.38	7.15
	232	293.40	0.0094	0.0297	16.0940	0.0486	2.7364	2.8840	0.4133	0.2057	0.0785	0.2842	0.4801	0.6298	3.52	10.86
	239	330.67	0.0097	0.0254	19.5265	0.0468	3.2445	2.6971	0.4172	0.1720	0.1786	0.3506	0.5658	0.5928	3.02	7.35
	250	299.68	0.0104	0.0263	16.0117	0.0449	2.8277	2.8962	0.5021	0.1929	0.1301	0.3230	0.5258	0.4827	5.46	8.32
	257	348.48	0.0106	0.0298	22.8121	0.0479	3.0446	2.8008	0.4820	0.1934	0.1614	0.3548	0.5225	0.6310	5.00	6.88
	267	325.02	0.0103	0.0300	18.7668	0.0374	2.8845	2.7712	0.4398	0.2674	0.1702	0.4376	0.7088	0.7515	4.43	8.23
16	140	260.17	0.0083	0.0237	14.1313	0.0444	2.6644	2.4274	0.3547	0.1421	0.1250	0.2671	0.4570	0.3967	3.38	8.75
	149	230.84	0.0088	0.0262	11.9581	0.0395	2.0354	2.6111	0.3138	0.1443	0.1234	0.2677	0.1659	0.3684	2.99	7.87
	158	254.01	0.0085	0.0249	12.7527	0.0516	2.3124	2.8141	0.3623	0.1422	0.0906	0.2328	0.3618	0.4678	4.77	8.00
	167	226.14	0.0074	0.0200	11.9257	0.0433	2.0480	2.3887	0.3455	0.1643	0.0925	0.2568	.[j]	0.3378	2.82	8.07
	176	295.37	0.0113	0.0230	16.0468	0.0539	3.0134	2.7385	0.3915	0.1911	0.1600	0.3511	0.4521	0.5135	3.90	10.80
	186	281.14	0.0098	0.0255	15.7303	0.0563	3.2833	2.6922	0.4170	0.2165	0.1332	0.3497	0.4862	0.4876	3.43	12.78
	195	258.00	0.0082	0.0278	13.1759	0.0377	2.4408	2.4968	0.3732	0.1605	0.1218	0.2823	0.3575	0.4117	2.99	6.78
	204	242.97	0.0087	0.0204	14.0914	0.0323	2.5294	2.3517	0.3741	0.2117	0.0705	0.2822	0.1204	0.4396	3.20	9.24
	213	271.42	0.0089	0.0209	16.2752	0.0493	2.6962	2.5244	0.3533	0.1911	0.1066	0.2977	0.4820	0.4117	3.76	13.10
	222	264.04	0.0082	0.0255	15.0096	0.0365	2.7510	2.7191	0.4025	0.2175	0.1027	0.3202	0.4730	0.4632	3.01	8.36
	231	251.29	0.0083	0.0219	14.8029	0.0445	2.5183	3.1639	0.4066	0.1731	0.0895	0.2626	0.2620	0.3864	2.73	8.98
	240	312.12	0.0106	0.0241	20.3758	0.0501	3.3832	2.6137	0.3606	0.1402	0.1294	0.2696	0.2648	0.4492	2.61	15.51
	249	282.84	0.0108	0.0208	15.5000	0.0417	2.5402	2.7903	0.3922	0.0912	0.1603	0.2515	0.5363	0.7025	3.66	5.99
	258	292.75	0.0116	0.0302	16.2961	0.0708	3.3319	2.8636	0.5374	0.3022	0.2022	0.5044	0.3951	0.5279	4.09	5.60
	266	310.27	0.0092	0.0281	16.7564	0.0441	3.3700	2.8096	0.3282	0.2801	0.2046	0.4847	0.1550	0.4752	3.66	12.50

(continued)

Table A-10. Individual F_1 Male Necropsy Weights and Hormone Data (page 9 of 10)

Group[a]	Animal ID	Sacrifice Wt. (g)	Pituitary Wt. (g)	Thyroid Wt. (g)	Liver Wt. (g)	Paired Adrenal Gland Wt. (g)	Paired Kidney Wt. (g)	Paired Testis Wt. (g)	Paired Epididymis Wt. (g)	Ventral Prostate Wt. (g)	Dorso-lateral Prostate Wt. (g)	Prostate Wt. (g)	Seminal Vesicles with Coagulating Glands	LABC[b] Muscle Complex Wt. (g)	Thyroxine (ug/dL)	Thyroid Stimulating Hormone (ng/ml)
17	143	273.85	0.0118	0.0327	17.4827	0.0525	2.6100	2.6287	0.3848	0.2413	0.1351	0.3764	0.4640	0.5216	6.87	13.78
	146	299.66	0.0104	0.0252	19.4050	0.0397	3.2166	2.6791	0.3959	0.1732	0.1532	0.3264	0.7568	0.5670	6.46	9.35
	161	300.98	.[h]	0.0408	20.3494	0.0494	2.6725	2.6065	0.3874	0.1532	0.1640	0.3172	0.5862	0.4875	7.38	13.54
	164	329.63	0.0085	0.0380	21.1594	0.0517	2.8652	2.8191	0.4368	0.3024	0.1636	0.4660	0.7494	0.6194	6.44	10.97
	179	319.42	0.0115	0.0385	18.3210	0.0560	3.0156	2.8640	0.4528	0.3413	0.1680	0.5093	0.7000	0.6032	5.88	21.09
	189	301.96	0.0101	0.0372	18.3697	0.0724	3.3204	2.5850	0.4861	0.2920	0.1191	0.4111	0.5548	0.5884	5.11	20.13
	192	350.01	0.0106	0.0352	23.1780	0.0524	3.2665	2.8597	0.4565	0.2903	0.1411	0.4314	0.6508	0.6614	3.93	14.16
	207	293.91	0.0123	0.0254	19.4894	0.0643	3.0786	2.7945	0.4300	0.3252	0.1870	0.5122	0.6488	0.6695	5.47	27.72
	210	273.90	0.0061	0.0265	18.1859	0.0442	2.4734	2.5635	0.4274	0.1835	0.0852	0.2687	0.5686	0.5279	4.58	18.00
	225	334.96	0.0090	0.0330	22.0598	0.0678	3.2548	2.5916	0.4671	0.2399	0.2323	0.4722	0.3421	0.7889	5.40	12.55
	228	320.45	0.0117	0.0274	21.3093	0.0492	3.1297	2.7863	0.4363	0.2814	0.1172	0.3986	1.0679	0.6373	3.82	22.24
	243	385.09	0.0067	0.0293	27.6322	0.0528	3.8360	2.9371	0.4706	0.3602	0.1730	0.5332	0.7584	0.6156	5.81	27.64
	246	283.85	0.0144	0.0257	19.1822	0.0439	2.6191	2.7855	0.4704	0.1554	0.1287	0.2841	0.4876	0.5553	5.80	13.36
	261	308.31	0.0112	0.0299	19.2691	0.0526	3.0840	3.1979	0.5855	0.4097	0.2957	0.7054	0.6243	0.6569	5.53	12.10
	263	305.11	0.0123	0.0330	19.7582	0.0449	3.4090	2.8572	0.4737	0.4088	0.1145	0.5233	0.6549	0.5975	6.43	8.86
18	144	265.71	0.0100	0.0291	19.6582	0.0495	2.6840	2.1776	0.3720	0.1971	0.2072	0.4043	0.3804	0.4591	6.19	9.45
	145	284.21	0.0107	0.0383	21.4656	0.0225	2.7613	2.5154	0.2891	0.1990	0.1757	0.3747	0.4779	0.5153	6.39	27.86
	162	281.88	0.0102	0.0209	17.8585	0.0469	2.6733	2.7159	0.4086	0.1806	0.1230	0.3036	0.6415	0.4582	5.31	25.80
	163	310.28	0.0115	0.0303	22.7501	0.0443	3.0806	2.7456	0.4134	0.2555	0.2196	0.4751	0.5861	0.5198	6.12	6.91
	180	280.63	0.0100	0.0344	20.0776	0.0397	2.7880	2.5379	0.3080	0.1997	0.1965	0.3962	0.3247	0.4841	7.05	9.43
	181	258.14	0.0083	0.0346	16.7381	0.0658	2.4313	2.7614	0.3919	0.1750	0.0835	0.2585	0.3812	0.4243	6.08	11.05
	190	272.49	0.0101	0.0257	19.8510	0.0411	2.8755	2.8303	0.4188	0.1711	0.1149	0.2860	0.4023	0.4646	5.79	15.61
	191	278.03	0.0106	0.0238	20.0250	0.0547	3.0560	2.4089	0.4790	0.2450	0.2494	0.4944	0.3641	0.6640	5.17	11.12
	208	279.73	0.0105	0.0340	20.7203	0.0467	3.0073	2.7213	0.4388	0.2552	0.1534	0.4086	0.3827	0.4431	6.37	10.74
	209	314.58	0.0121	0.0395	22.6696	0.0546	3.4696	2.8889	0.4950	0.3205	0.2615	0.5820	0.4382	0.7720	5.32	15.89
	226	340.04	0.0105	0.0353	25.1465	0.0482	3.4563	2.3825	0.3738	0.1525	0.0876	0.2401	0.4928	0.4932	5.07	12.01
	227	312.83	.[h]	0.0361	25.1488	0.0534	3.3847	3.0764	0.4315	0.2878	0.2268	0.5146	0.7653	0.5247	4.77	15.60
	244	352.47	.[h]	0.0337	26.8862	0.0686	3.3225	2.7033	0.4442	0.2689	0.1843	0.4532	0.7167	0.5099	5.62	20.02
	245	327.11	0.0105	0.0363	26.1542	0.0453	3.0440	2.6680	0.4119	0.1042	0.1789	0.2831	0.4799	0.5948	5.30	17.46
	262	296.28	0.0107	0.0362	22.4525	0.0439	2.7181	2.5148	0.3624	0.2185	0.2454	0.4639	0.4752	0.5505	5.35	8.03

(continued)

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.
[b]Levator ani plus bulbcavernosus muscle complex.
[c]Body weight was inadvertently not recorded prior to blood being taken.
[d]Male was removed from the study because his correct postnatal day 0 could not be confirmed.
[e]Male was removed from the study because it was not dosed on the correct postnatal days.
[f]Male was found dead on postnatal day 37 after dosing (misdirected dose).
[g]Male was euthanized on postnatal day 29 after dosing due to a leg injury.
[h]Organ weight was a statistical outlier and therefore it was excluded.
[i]Adrenal gland was inadvertently lost prior to being weighed.
[j]Seminal vesicles with coagulating glands was inadvertently nicked and leaked prior to weighing and therefore the weight was excluded.
[k]Levator ani plus bulbcavernosus muscle complex was inadvertently not completely removed from the animal and therefore the weight was excluded.
[l]Male was found dead on postnatal day 31 prior to dosing (misdirected dose).
[m]Value was below the minimum detection limit.
[n]Weight was inadvertently not recorded.
[o]Male was found dead on postnatal day 50 prior to dosing.
[p]Male was found dead on postnatal day 37 prior to dosing (misdirected dose).
[q]Value could not be determined since the ventral prostate weight was a statistical outlier and therefore it was excluded.
[r]The blood tube was accidentally dropped therefore no sample was available for this animal.

Table A-11. Individual F_1 Male Necropsy Findings (page 1 of 5)

A. Scheduled Necropsy

Group[a]	Animal ID	Necropsy Finding
1	15	Kidney: hydronephrosis, right
2	101	Testis: undescended, left
		Testis: reduced in size, left
		Epididymis: reduced in size, left
	133	Kidney: hydronephrosis, right
3	13	Kidney: hydronephrosis, right
	91	Kidney: hydronephrosis, right
4	12	Kidney: hydronephrosis, right
5	7	Chromodacryorrhea: nose
	26	Intestines: distended with air
	39	Kidney: hydronephrosis, bilateral
	44	Kidney: hydronephrosis, right
	98	Kidney: hydronephrosis, right
	116	Kidney: hydronephrosis, right
6	8	Kidney: hydronephrosis, right
	11	Kidney: hydronephrosis, right
	22	Kidney: hydronephrosis, right
	61	Kidney: hydronephrosis, right
7	10	Kidney: hydronephrosis, right
	42	Kidney: hydronephrosis, right
	59	Kidney: hydronephrosis, right
		Seminal Vesicles: reduced in size
9	89	Kidney: hydronephrosis, right
10	199	Urinary Bladder: multiple 1 to 3 mm calculi and wall thickened

(continued)

A. Scheduled Necropsy

Group[a]	Animal ID	Necropsy Finding
11	152	Thyroid: enlarged and darkened, left side
	170	Thyroid: enlarged and darkened
	173	Kidney: hydronephrosis, right
		Thyroid: darkened and right side enlarged
	183	Thyroid: enlarged
	198	Thyroid: enlarged, bilateral
	201	Thyroid: enlarged
	219	Ventral Prostate: reduced in size
		Dorsolateral Prostate: reduced in size
		Seminal Vesicles: reduced in size, bilateral
		Thyroid: enlarged and reddened, bilateral
	237	Thyroid: enlarged and reddened
	252	Thyroid: enlarged
	269	Lungs: multiple foci
12	138	Thyroid: enlarged
	151	Thyroid: enlarged, bilateral
	156	Thyroid: enlarged and reddened, bilateral
	169	Kidney: hydronephrosis, right
		Thyroid: enlarged and reddened, bilateral
	174	Liver: reduced in size
		Thyroid: enlarged and reddened, bilateral
	184	Thyroid: enlarged and reddened, bilateral
	197	Liver: mottled
		Thyroid: enlarged, bilateral
	202	Thyroid: enlarged and reddened, bilateral
		Pituitary: reduced in size
	215	Adrenal Gland: reduced in size, bilateral
		Thyroid: enlarged
	220	Adrenal Gland: reduced in size, bilateral
		Thyroid: enlarged, bilateral
	233	Kidney: hydronephrosis, right
		Liver: mottled
		Thyroid: enlarged, bilateral
	238	Liver: reduced in size
		Adrenal Gland: reduced in size, bilateral
		Kidney: reduced in size, bilateral
		Thyroid: enlarged and reddened
	251	Liver: reduced in size
		Ventral Prostate: reduced in size
		Dorsolateral Prostate: reduced in size
		Thyroid: enlarged and reddened

(continued)

A. Scheduled Necropsy

Group[a]	Animal ID	Necropsy Finding
12	256	Liver: reduced in size Adrenal Gland: reduced in size, bilateral Thyroid: enlarged and reddened
13	177	Seminal Vesicles: reduced in size Dorsolateral Prostate: reduced in size
	194	Adrenal Gland: dark tan/brown, bilateral
	205	Adrenal Gland: pale, bilateral
	212	Adrenal Gland: enlarged, bilateral
	223	Kidney: hydronephrosis, right
	230	Adrenal Gland: pale, bilateral
14	160	Kidney: hydronephrosis, right
	178	Adrenal Gland: enlarged, bilateral
	188	Adrenal Gland: enlarged, bilateral
	193	Adrenal Gland: enlarged, bilateral
	206	Ventral Prostate: reduced in size Dorsolateral Prostate: reduced in size Seminal Vesicles: reduced in size, bilateral Adrenal Gland: enlarged, bilateral
	211	Ventral Prostate: reduced in size Seminal Vesicle: reduced in size Adrenal Gland: enlarged, bilateral
	224	Seminal Vesicles: reduced in size
	229	Seminal Vesicles: reduced in size, bilateral Ventral Prostate: reduced in size
	247	Lung: pinpoint foci, right
	264	Kidney: hydronephrosis, right Adrenal Gland: enlarged, left
15	139	Seminal Vesicles: reduced in size, bilateral Ventral Prostate: reduced in size
	196	Seminal Vesicle: reduced in size, right
	214	Ventral Prostate: reduced in size Dorsolateral Prostate: reduced in size
	232	Seminal Vesicles: reduced in size, bilateral Dorsolateral Prostate: reduced in size

(continued)

A. Scheduled Necropsy

Group[a]	Animal ID	Necropsy Finding
16	149	Seminal Vesicles: reduced in size
	158	Seminal Vesicles: reduced in size, bilateral
		Ventral Prostate: reduced in size
		Dorsolateral Prostate: reduced in size
	195	Seminal Vesicles: reduced in size, bilateral
		Ventral Prostate: reduced in size
		Dorsolateral Prostate: reduced in size
		Pituitary: reduced in size
	204	Ventral Prostate: reduced in size
		Dorsolateral Prostate: reduced in size
		Seminal Vesicles: reduced in size
	231	Seminal Vesicles: reduced in size
	240	Seminal Vesicles: reduced in size
	249	Ventral Prostate: reduced in size
	258	Spleen: enlarged with white foci
		Lungs: multiple reddened areas
		Kidney: hydronephrosis, right
17	164	Kidney: hydronephrosis, right
	210	Ventral Prostate: reduced in size
		Dorsolateral Prostate: reduced in size
		Seminal Vesicles: reduced in size, bilateral
	246	Kidney: hydronephrosis, right
18	163	Kidney: hydronephrosis, right
	181	Seminal Vesicles: reduced in size
		Dorsolateral Prostate: reduced in size
	208	Kidney: hydronephrosis, right
18	226	Ventral Prostate: reduced in size
		Dorsolateral Prostate: reduced in size
		Seminal Vesicles: reduced in size, bilateral
	245	Ventral Prostate: reduced in size
		Seminal Vesicles: reduced in size

(continued)

B. Unscheduled Necropsy

Group[a]	Animal ID	Necropsy Finding
2	54	Misdirected dose
4	20	Left metatarsal extremely swollen and edematous with ankle scabbed over and venous return appeared constricted by underlying tissue
10	217	Lungs: congested and oil present on cut surface, misdirected dose
12	268	Trachea: oil present
14	242	Lungs: congested, dark red, small amount of corn oil on cut surface, misdirected dose

[a]Dose groups are as follows: 1 is 0 mg/kg/day; 2 is 75 mg/kg/day Atrazine; 3 is 150 mg/kg/day Atrazine; 4 is 50 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 5 is 100 mg/kg/day of p,p'-Dichlorodiphenyldichloroethane; 6 is 30 mg/kg/day of Vinclozolin; 7 is 100 mg/kg/day of Vinclozolin; 8 is 25 mg/kg/day of Methoxychlor; 9 is 50 mg/kg/day of Methoxychlor; 10 is 0 mg/kg/day; 11 is 2 mg/kg/day of Propylthiouracil; 12 is 25 mg/kg/day of Propylthiouracil; 13 is 50 mg/kg/day of Ketoconazole; 14 is 100 mg/kg/day of Ketoconazole; 15 is 50 mg/kg/day of Linuron; 16 is 100 mg/kg/day of Linuron; 17 is 50 mg/kg/day of Phenobarbital and 18 is 100 mg/kg/day of Phenobarbital. Groups 1 through 9 were in component 1 and groups 10 through 18 were in component 2.

Table B-1. Summary of the F_0 Reproductive and Lactational Indexes of the Untreated Females for the F_1 Litters (page 1 of 2)

No. of Females	
No. of Pregnant Females	48[a]
No. of Females with Live Litters (pnd 0)	48
Gestational Index (no. females with live litters/no. females pregnant)	100.0
Gestational Length (days)[b]	21.8 ± 0.1 N=48
No. of Live Litters:	
Postnatal Day 0	48
Postnatal Day 4	48
Postnatal Day 7	48
Postnatal Day 14	48
Postnatal Day 21	48
Number of Live Pups on Postnatal Day 0[b]	12.6 ± 0.3 N=48
Number of Dead Pups on Postnatal Day 0[b]	0.1 ± 0.1 N=48
Total Number of Pups on Postnatal Day 0[b]	12.7 ± 0.3 N=48
Stillbirth Index (no. dead on pnd 0/total no. on pnd 0)[b]	1.4 ± 0.7 N=48

(continued)

Table B-1. Summary of the F_0 Reproductive and Lactational Indexes of the Untreated Females for the F_1 Litters (page 2 of 2)

Live Birth Index (no. live on pnd 0/total no. on pnd 0)[b]	98.6 ± 0.8 N=48
4 Day Survival Index (no. surviving 4 days/no. live on pnd 0)[b]	99.1 ± 0.4 N=48
7 Day Survival Index (no. surviving 7 days/no. live on pnd 4)[b]	100.0 ± 0.0 N=48
14 Day Survival Index (no. surviving 14 days/no. live on pnd 7)[b]	100.0 ± 0.0 N=48
21 Day Survival Index (no. surviving 21 days/no. live on pnd 14)[b]	99.7 ± 0.3 N=48
Lactational Index (no. surviving 21 days/no. live on pnd 4)[b]	99.7 ± 0.3 N=48

[a]Females 4 and 12 were removed from the study because their correct postnatal day 0 could not be confirmed.
[b]Reported as the mean ± S.E.M.; pnd=postnatal day. All indexes are the average percent per litter.

Table B-2. Summary of the F_1 Litter Size, Pup Body Weights, and Percent Male Pups During Lactation from the F_0 Untreated Females (page 1 of 3)

No. of Live Litters:	
Postnatal Day 0	48
Postnatal Day 4	48
Postnatal Day 7	48
Postnatal Day 14	48
Postnatal Day 21	48
Average Number of Live Pups per Litter (pnd 0)[a]	12.6 ± 0.3 N=48
Average Number of Live Pups per Litter (pnd 4)[a]	12.5 ± 0.3 N=48
Average Number of Live Pups per Litter (pnd 7)[a]	9.7 ± 0.1 N=48
Average Number of Live Pups per LItter (pnd 14)[a]	9.7 ± 0.1 N=48
Average Number of Live Pups per Litter (pnd 21)[a]	9.7 ± 0.2 N=48
Average Pup Body Weight (g) per Litter (pnd 0)[a]	6.63 ± 0.08 N=48
Average **Male** Body Weight (g) per Litter (pnd 0)[a]	6.78 ± 0.08 N=47[b]
Average **Female** Body Weight (g) per Litter (pnd 0)[a]	6.44 ± 0.08 N=48

(continued)

Table B-2. Summary of the F_1 Litter Size, Pup Body Weights, and Percent Male Pups During Lactation from the F_0 Untreated Females (page 2 of 3)

Average Pup Body Weight (g) per Litter (pnd 4)[a]	10.79 ± 0.15 N=48
Average **Male** Body Weight (g) per Litter (pnd 4)[a]	11.03 ± 0.16 N=47[b]
Average **Female** Body Weight (g) per Litter (pnd 4)[a]	10.48 ± 0.16 N=48
Average Pup Body Weight (g) per Litter (pnd 7)[a]	17.22 ± 0.25 N=48
Average **Male** Body Weight (g) per Litter (pnd 7)[a]	17.50 ± 0.25 N=47[b]
Average **Female** Body Weight (g) per Litter (pnd 7)[a]	16.67 ± 0.28 N=44[c]
Average Pup Body Weight (g) per Litter (pnd 14)[a]	33.97 ± 0.46 N=48
Average **Male** Body Weight (g) per Litter (pnd 14)[a]	34.43 ± 0.47 N=47[b]
Average **Female** Body Weight (g) per Litter (pnd 14)[a]	33.14 ± 0.50 N=44[c]

(continued)

Table B-2. Summary of the F_1 Litter Size, Pup Body Weights, and Percent Male Pups During Lactation from the F_0 Untreated Females (page 3 of 3)

Average Pup Body Weight (g) per Litter (pnd 21)[a]	55.89 ± 0.83 N=48
Average **Male** Body Weight (g) per Litter (pnd 21)[a]	56.81 ± 0.86 N=47[b]
Average **Female** Body Weight (g) per Litter (pnd 21)[a]	54.15 ± 0.89 N=44[c]
Percent Male Pups per Litter (pnd 0)[a]	51.5 ± 2.3 N=48
Percent Male Pups per Litter (pnd 4)[a]	51.5 ± 2.3 N=48

[a]Reported as the mean ± S.E.M.; pnd=postnatal day.
[b]Decrease in N is due to one litter having only female pups.
[c]Decrease in N is due to four litters having only male pups.

Table B-3. Summary of the Clinical Observations on Postnatal Days 0 Through 21 for the F_1 Pups from the F_0 Untreated Females (page 1 of 1)

Day[a]	Sex[b]	Clinical Observation	
0	F	Found dead	4
	M	Found dead	3
		No milk band	1
4	F	Missing and presumed dead	2
	M	Missing and presumed dead	4
		Tail: thread-like; Pup culled	1
14	F	Eye(s): not open	1
		Thin fur: back	3
	M	Tail: kinked	1
		Thin fur: back	3
21	F	Cannibalized, 1 x 2 cm piece of fur/skin only	1
		Eye(s): not open; Head: domed	1

[a]Postnatal day.
[b]F is female and M is male.

Table B-4. Summary of the Necropsy Findings on Postnatal Days 0 Through 21 for the F_1 Pups from the F_0 Untreated Females (page 1 of 1)

Day[a]	Sex[b]	Necropsy Finding	
0	F	Ductus open; Digestive tract too autolyzed to evaluate	1
		Ductus open; No air in lungs; No milk in stomach	2
		Necropsy inadvertently not performed	1
	M	Ductus open; Milk in stomach	1
		Ductus open; No air in lungs; No milk in stomach	1
		Placenta still attached; Ductus open; No air in lungs; No milk in stomach	1
21	F	Cannibalized, unable to evaluate	1

[a]Postnatal day.
[b]F is female and M is male.

Table B-5. Individual F_0 Untreated Female Reproductive and Lactational Indexes (page 1 of 2)

Female ID	Pregnant	Live Litter	Gestational Length	Live PND 0	Dead PND 0	Total PND 0	Live PND 4	Live PND 7	Live PND 14	Live PND 21
2[a]	Yes	Yes	22	13	0	13	13	10	10	10
4[b]										
6	Yes	Yes	22	15	0	15	15	10	10	10
8	Yes	Yes	22	12	0	12	12	10	10	10
10	Yes	Yes	22	15	0	15	15	10	10	10
12[b]										
14	Yes	Yes	22	15	0	15	15	10	10	10
16	Yes	Yes	21	15	1	16	15	10	10	10
18	Yes	Yes	22	13	0	13	12	10	10	10
20	Yes	Yes	22	15	0	15	15	10	10	10
22	Yes	Yes	22	10	1	11	10	10	10	10
24	Yes	Yes	21	10	0	10	10	10	10	10
26	Yes	Yes	22	11	0	11	10	10	10	10
28	Yes	Yes	22	12	1	13	12	10	10	10
30	Yes	Yes	22	7	1	8	7	6	6	6
32	Yes	Yes	22	13	0	13	13	10	10	10
34	Yes	Yes	22	15	0	15	15	10	10	10
36	Yes	Yes	22	12	0	12	12	10	10	10
38	Yes	Yes	22	11	0	11	11	10	10	10
40	Yes	Yes	22	6	3	9	6	6	6	6
42	Yes	Yes	22	12	0	12	12	10	10	10
44	Yes	Yes	22	9	0	9	9	9	9	9
46	Yes	Yes	22	6	0	6	6	6	6	5
48	Yes	Yes	22	14	0	14	14	10	10	10
50	Yes	Yes	22	13	0	13	13	10	10	10
52	Yes	Yes	22	13	0	13	13	10	10	10
54	Yes	Yes	22	14	0	14	14	10	10	10
56	Yes	Yes	22	15	0	15	14	10	10	10
58	Yes	Yes	22	13	0	13	13	10	10	10
60	Yes	Yes	21	13	0	13	12	10	10	10
62	Yes	Yes	22	13	0	13	13	10	10	10
64	Yes	Yes	22	14	0	14	14	10	10	10
66	Yes	Yes	22	13	0	13	13	10	10	10
68	Yes	Yes	22	14	0	14	14	10	10	10
70	Yes	Yes	21	15	0	15	15	10	10	10
72	Yes	Yes	22	12	0	12	12	10	10	10
74	Yes	Yes	22	15	0	15	15	10	10	10
76	Yes	Yes	21	13	0	13	13	10	10	10
78	Yes	Yes	21	11	0	11	11	10	10	10

(continued)

Table B-5. Individual F_0 Untreated Female Reproductive and Lactational Indexes (page 2 of 2)

Female ID	Pregnant	Live Litter	Gestational Length	Live PND 0	Dead PND 0	Total PND 0	Live PND 4	Live PND 7	Live PND 14	Live PND 21
80	Yes	Yes	22	16	0	16	16	10	10	10
82	Yes	Yes	22	12	0	12	12	10	10	10
84	Yes	Yes	22	14	0	14	13	10	10	10
86	Yes	Yes	22	11	0	11	11	10	10	10
88	Yes	Yes	21	13	0	13	13	10	10	10
90	Yes	Yes	21	13	0	13	13	10	10	10
92	Yes	Yes	21	13	0	13	13	10	10	10
94	Yes	Yes	22	16	0	16	15	10	10	10
96	Yes	Yes	22	11	0	11	11	10	10	10
98	Yes	Yes	22	15	0	15	15	10	10	10
100	Yes	Yes	21	8	0	8	8	8	8	8

[a]Females 2 through 50 were in component 1 and females 52 through 100 were in component 2.
[b]Female was removed from the study because her correct postnatal day 0 could not be confirmed.

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 1 of 16)

Female ID	Sex	Postnatal Day				
		0	4	7	14	21
2[b]	M	6.70	11.15	16.69	28.80	53.16
		6.69	10.62	15.98	31.67	52.97
		6.81	11.53	15.53	29.51	54.30
		7.37	10.68	17.51	31.89	58.32
		6.14	10.69	16.72	31.56	46.80
	F	6.41	9.70	16.17	29.23	50.02
		6.57	10.78	15.13	31.21	51.77
		6.46	10.31	15.17	31.36	52.88
		6.05	10.47	14.47	31.42	49.40
		6.22	10.81	16.12	30.67	53.23
		6.56	10.82			
		5.97	10.44			
		6.35	10.98			
4[c]						
6	M	7.66	12.26	18.68	39.33	60.49
		7.16	10.48	19.58	38.88	64.44
		7.57	11.04	19.72	34.71	58.85
		7.56	12.25	20.09	38.16	65.20
		7.07	11.66	19.40	37.24	61.61
		6.10	10.90	18.81	38.24	64.58
		7.05	12.22	17.79	38.37	65.86
		7.02	10.80	20.17	36.05	65.27
		7.43	11.14	18.33	37.02	62.77
		7.39	12.13	19.93	37.44	65.47
		6.86	11.74			
		6.84	10.47			
		7.36	9.96			
		7.16				
	F	6.93	10.36			
		.[d]	10.93			
8	M	6.40	10.95	11.95	33.36	56.78
		7.21	11.35	16.80	36.41	59.24
		7.62	12.30	16.53	35.50	58.23
		7.02	11.42	17.96	27.36	60.03
		6.63	10.71	19.16	33.09	56.56
		4.31	7.33	18.10	33.39	59.99
		6.88	11.57	19.06	35.45	46.90
		7.12	11.95	18.34	35.40	56.40
	F	7.26	10.51	17.95	36.27	57.96
		5.97	9.59	17.99	35.65	59.44
		7.10	11.96			
		6.52	11.69			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 2 of 16)

Female ID	Sex	Postnatal Day				
		0	4	7	14	21
10	M	7.02	7.50	17.46	34.17	55.98
		6.70	10.96	15.93	34.41	55.25
		5.98	11.19	17.93	34.00	56.92
		6.84	10.57	18.50	32.93	52.47
		6.52	11.16	17.16	31.04	50.80
		6.73	10.48	16.18	34.71	55.96
		6.72	11.44	16.73	29.83	57.74
		.[d]	10.60	18.00	32.33	55.27
	F	5.66	10.35	16.82	27.58	51.20
		6.69	10.67	14.73	31.32	46.65
		6.74	10.55			
		6.69	10.73			
		6.50	10.91			
		6.47	8.92			
		6.86	10.52			
		6.88				
12[c]						
14	M	6.48	10.46	17.35	35.32	59.89
		6.96	10.74	17.96	36.38	60.82
		6.47	10.39	17.49	34.80	57.57
		6.78	9.91	16.95	34.94	58.64
		6.65	10.34	17.08	36.55	57.97
		6.45	10.29	16.85	35.39	61.35
		6.44	10.01	18.13	36.13	58.88
		6.73	10.00	16.99	35.30	61.34
		6.91	9.90	17.25	35.46	56.79
	F	6.72	10.06	17.12	34.94	56.34
		6.54	10.38			
		6.18	10.20			
		6.52	9.74			
		6.10	10.12			
		6.11	10.37			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 3 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
16	M	6.55	9.60	13.59	26.88	44.30
		7.04	9.40	16.40	29.56	38.89
		6.86	10.89	13.62	30.03	45.16
		7.27	9.53	17.01	25.66	47.97
		6.64	8.19	14.86	31.82	42.21
		6.87	10.13	15.47	29.27	47.38
		6.65	10.09	15.52	27.96	41.91
		7.21	8.95	12.30	31.38	41.39
		6.34	10.13	16.19	28.73	43.14
	F	6.52	10.11	16.33	30.23	45.73
		6.31	9.89			
		6.00	9.69			
		6.15	7.94			
		6.31	8.90			
		6.38	10.07			
18	M	7.90	11.59	19.56	33.41	54.03
		6.92	12.32	18.93	31.81	56.69
		7.06	12.38	19.33	32.82	57.07
		7.90				
		7.29	.[e]			
	F	6.88	10.82	16.94	32.30	56.46
		6.66	9.58	17.18	33.53	49.84
		6.95	11.26	18.11	33.66	51.79
		7.37	12.31	18.12	31.81	53.90
		6.80	10.81	17.41	30.76	52.50
		6.91	11.18	18.45	30.55	52.67
		6.97	11.77	18.27	33.25	54.81
		6.49	11.29			
		.[d]	11.58			
20	M	7.37	11.15	17.83	37.17	60.63
		7.00	10.98	19.33	35.17	55.49
		6.70	11.44	18.71	32.33	55.99
		6.83	10.25	17.85	35.12	60.35
		6.59	11.46	18.85	35.14	59.14
		7.39	10.78	17.48	34.72	58.43
		7.26	11.15	18.96	35.33	57.26
		7.31	11.25	17.21	36.77	50.24
		6.66	10.66	18.62	35.70	52.33
	F	7.30	11.36	17.32	34.44	58.76
		6.60	11.53			
		7.03	10.84			
		7.07	6.97			
		5.75	10.59			
		6.69	11.09			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 4 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
22	M	7.48	12.28	18.35	34.36	60.31
		5.56	12.85	19.08	35.15	55.25
		7.67	12.39	18.04	34.89	60.07
		7.58	12.67	18.37	35.89	60.61
		7.54	12.45	18.77	35.64	58.12
		7.39	12.52	18.31	33.09	58.78
		7.87				
	F	7.87	8.28	16.86	34.67	41.04
		7.00	11.44	18.44	32.53	58.51
		7.61	12.12	17.37	34.64	54.29
		.[d]	11.69	12.49	27.71	57.35
24	M	6.18	9.98	13.74	24.51	37.88
		6.13	9.62	13.21	24.70	38.28
		6.08	10.13	14.70	23.50	38.77
		5.74	9.43	14.12	24.20	39.30
		5.89	9.39	13.46	23.90	36.87
	F	4.60	7.71	13.33	22.61	35.55
		5.13	6.41	9.29	22.01	32.70
		5.09	9.17	12.17	20.40	34.78
		5.60	8.48	11.66	22.50	36.41
		5.16	8.75	10.48	18.70	30.24
26	M	7.76	12.43	17.60	33.97	51.71
		7.74	12.70	18.43	32.68	53.47
		7.55	11.71	17.70	31.46	55.93
		7.73	11.48	18.28	33.36	56.85
		7.24	11.90	17.57	32.29	54.53
		.[d]	12.25	16.68	32.46	58.42
	F	7.06	11.69	17.61	29.32	47.61
		7.23	11.83	16.92	31.78	53.07
		7.06	11.72	15.26	31.80	52.45
		7.16	10.41	17.38	31.36	51.82
		6.82				
		6.85	.[e]			
28	M	7.00	11.60	17.89	38.98	63.07
		7.18	11.86	18.29	37.59	57.17
		7.08	11.09	15.78	37.32	61.98
		6.68	10.85	16.11	34.00	58.72
		6.98	11.02	18.53	37.00	62.65
		7.40	9.79	19.29	37.07	64.19
		7.86	8.94	17.95	34.14	55.80
	F	6.52	10.29	16.97	34.49	58.95
		6.29	10.12	16.79	35.29	53.79
		6.52	10.19	16.62	35.05	58.20
		6.16	10.50			
		6.42	9.92			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 5 of 16)

Female ID	Sex	Postnatal Day				
		0	4	7	14	21
30	M	8.02	14.19	21.35	40.62	67.61
		8.26	13.93	22.19	42.18	69.55
		8.68	13.53	.[f]		
	F	7.41	12.58	20.29	39.72	66.16
		7.53	12.36	20.93	39.09	63.96
		7.76	12.65	19.73	39.55	63.81
		7.45	13.31	19.44	37.66	65.29
32	M	7.41	12.24	16.03	35.05	56.29
		7.21	10.26	18.16	33.66	57.03
		7.54	11.02	17.84	33.65	59.47
		7.09	11.74	15.83	33.94	57.49
		6.23	11.74	17.11	32.55	58.73
		7.97	10.33	18.17	31.86	53.61
	F	6.78	11.16	16.84	32.71	50.29
		6.95	9.30	14.78	31.18	52.18
		6.37	10.43	16.24	33.05	53.55
		6.67	10.79	16.20	30.16	51.23
		6.79	11.02			
		7.00	10.84			
		5.47	10.73			
34	M	7.47	10.85	18.45	35.83	56.42
		6.81	9.61	17.16	35.18	57.15
		6.61	11.13	16.54	32.80	56.34
		7.84	11.41	15.50	34.63	55.94
		7.25	10.34	18.30	33.98	54.94
		7.09	10.26	16.79	33.17	61.68
		.[d]	10.50	16.97	34.19	59.89
		.[d]	10.42	12.43	33.49	54.89
	F	7.00	10.13	17.05	31.92	56.52
		6.45	10.32	15.81	33.77	55.13
		7.23	10.74			
		6.79	9.68			
		5.51	9.05			
		7.27	10.15			
		6.90	10.05			
		7.02				
		6.36				

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 6 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
36	M	8.03	10.73	16.96	34.29	56.26
		7.46	10.25	16.74	32.24	55.87
		7.05	11.03	15.57	33.50	56.79
		7.19	10.84	16.67	34.19	56.19
		7.11	10.91	17.16	33.02	55.17
	F	7.06	10.59	15.76	33.95	54.16
		7.32	11.17	16.02	32.50	51.46
		7.12	10.07	15.54	32.46	54.70
		7.25	10.22	17.20	33.06	54.40
		6.14	10.01	16.56	33.26	52.94
		7.12	9.15			
		6.48	10.70			
38	M	7.21	11.51	17.91	34.89	52.87
		7.08	11.88	17.59	34.39	52.15
		7.09	12.13	18.82	33.89	54.38
		6.46	11.59	19.65	37.26	57.43
		.[d]	12.59	18.11	34.36	58.98
	F	6.98	12.17	18.31	33.61	56.85
		6.77	11.56	18.16	36.18	55.16
		6.81	11.74	18.14	36.04	56.48
		7.73	11.91	18.19	34.70	55.91
		7.11	11.39	18.82	34.76	56.89
		6.57	12.18			
		6.95				
40	M	7.11	11.95	20.11	41.60	68.01
		7.07	12.13	19.66	37.85	69.65
		.[d]	12.33	18.76	41.76	65.38
	F	6.75	11.95	18.18	39.45	64.98
		5.35	9.29	19.52	38.58	66.26
		6.07	11.10	15.40	35.02	57.22
		7.09				
42	M	8.01	12.91	19.94	35.00	57.24
		7.74	12.63	19.86	37.66	57.86
		8.17	12.50	19.78	37.20	60.51
		8.31	12.68	19.66	35.48	61.55
		8.02	12.70	19.37	37.84	58.71
		7.98	12.64	19.38	35.57	59.88
		7.74	12.70	18.78	36.93	59.96
		8.19	12.71	18.83	36.66	63.44
		8.02	12.60	19.23	36.50	57.89
		7.55	12.82	19.43	37.16	60.75
		7.17	12.50			
	F	7.18	11.97			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 7 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
44	M	6.41	12.44	17.03	35.29	56.06
		6.59	11.04	18.78	31.27	53.35
		7.20	11.62	16.29	31.25	50.19
		7.28				
	F	6.52	11.42	18.47	33.89	55.19
		6.97	11.10	16.45	31.78	53.22
		6.73	11.91	17.29	31.30	50.74
		6.58	10.80	17.90	32.52	52.69
		7.02	11.68	16.38	31.92	53.34
		.[d]	11.92	16.20	29.81	49.95
46	F	7.68	11.16	18.83	25.70	60.53
		8.26	13.21	18.76	35.59	58.28
		7.87	12.82	17.46	37.68	60.95
		7.23	12.37	18.63	34.75	53.53
		7.86	13.59	17.30	33.71	59.97
		7.97	12.69	20.14	35.25	.[g]
48	M	6.37	10.42	18.16	35.51	58.82
		6.20	11.20	17.76	35.71	59.84
		6.41	10.56	17.56	36.95	61.29
		6.46	10.92	18.23	36.99	58.54
		6.70	11.36	17.67	37.53	60.66
		6.49	11.78	17.86	36.13	59.71
	F	6.58	10.66	17.87	35.83	55.26
		6.25	10.50	17.33	34.42	55.53
		5.93	10.43	16.93	34.91	54.86
		5.75	10.45	17.56	34.20	55.55
		6.15	10.51			
		6.14	10.82			
		5.84	11.32			
		6.76	11.35			
50	M	7.51	11.35	19.26	31.68	59.85
		7.25	11.89	18.13	35.42	58.17
		6.79	11.30	19.03	35.11	58.28
		7.01	11.66	18.62	33.72	55.60
		6.89	11.10	19.12	34.16	58.76
		6.92	12.17	18.52	34.99	53.82
		7.28	10.09	17.17	34.56	60.77
		6.85	10.63	17.28	31.36	59.74
		7.48	11.12	16.74	35.76	54.02
		7.26	10.78	18.20	35.06	56.29
	F	5.27	8.35			
		5.86	8.93			
		6.47	9.62			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 8 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
52	M	7.51	12.08	17.86	37.80	59.69
		6.70	11.72	18.23	39.02	59.84
		7.13	12.05	17.28	38.35	57.65
		6.75	12.22	18.95	40.46	56.09
		6.63	12.27	19.48	36.97	62.80
		6.69	11.50	20.34	36.72	59.84
		7.37	11.36	19.36	38.81	57.92
		7.39	10.64	20.13	38.40	58.84
		.[d]	11.20	18.30	36.05	58.65
		.[d]	11.87	.[h]	37.97	63.21
	F	6.52	11.69			
		7.40	11.04			
		6.26	11.63			
		6.67				
		6.98				
54	M	6.54	10.75	18.03	34.49	56.06
		7.14	11.09	18.99	34.41	59.60
		6.10	11.35	18.92	37.31	59.88
		6.70	10.81	16.96	35.87	63.05
		6.86	11.33	17.70	35.56	62.46
		6.60	10.33	16.53	31.97	66.53
		6.80	11.20	18.41	34.66	63.83
		6.52	12.10	18.36	36.77	57.07
	F	6.00	11.60	17.92	32.57	63.36
		6.45	11.78	15.92	35.21	57.47
		6.77	10.96			
		6.32	11.14			
		6.07	9.40			
		6.84	9.99			
56	M	7.02	11.21	18.39	38.64	58.56
		6.56	10.63	19.54	37.16	64.27
		7.06	12.00	18.93	35.04	62.05
		6.78	12.15	19.43	37.57	60.68
		6.98	11.56	20.08	35.96	61.72
		6.25	11.75	17.37	38.39	61.53
		6.06				
		6.56	.[e]			
	F	6.53	10.69	18.55	34.75	56.29
		6.19	10.25	18.06	34.66	57.86
		6.10	10.20	16.44	32.04	55.02
		6.18	10.13	16.87	35.33	59.14
		6.44	9.81			
		5.93	10.60			
		5.90	11.72			
		.[d]	10.71			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 9 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
58	M	5.74	11.41	20.85	36.80	66.86
		6.99	11.43	19.78	42.69	60.32
		7.10	11.86	16.58	38.89	70.55
		7.20	11.92	19.06	40.56	62.70
		7.13	9.81	20.12	40.69	63.15
	F	6.97	8.32	15.33	37.56	56.95
		6.70	11.68	19.71	40.31	65.02
		7.07	11.34	18.09	34.22	58.38
		6.91	9.51	20.36	39.61	65.06
		5.28	10.91	19.73	40.52	64.82
		5.94	11.92			
		6.72	11.79			
		6.49	9.90			
60	M	5.90	9.54	6.30	29.59	50.63
		4.53	9.51	13.92	30.60	50.58
		5.50	9.68	15.93	32.89	48.90
		6.14	9.27	15.42	29.24	44.55
		5.71	8.65	14.89	32.06	47.12
		5.73	9.97	15.40	30.97	47.43
		5.75	.[e]			
	F	5.54	6.86	15.00	30.25	49.40
		5.62	9.07	14.24	26.06	40.25
		5.52	7.20	11.34	25.30	36.57
		5.77	9.03	12.56	31.41	50.32
		5.24	8.80			
		4.72	8.76			
62	M	6.33	11.34	15.35	35.58	59.23
		5.71	10.53	17.82	35.58	61.49
		6.44	10.28	16.51	35.97	60.79
		6.52	10.31	17.12	35.52	61.14
		6.29	10.85	16.68	34.81	56.89
		6.31	10.44	17.33	36.17	59.07
		6.08	9.40	17.35	37.08	59.80
		6.00	10.99	17.50	34.02	55.36
		6.20	10.74	17.95	35.88	55.36
	F	6.10	10.98	16.90	35.62	58.27
		5.81	9.96			
		6.24	9.56			
		5.88	10.37			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 10 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
64	M	6.87	10.88	18.70	36.20	60.61
		6.84	10.61	18.50	34.62	56.09
		6.49	10.44	18.78	35.02	57.39
		6.64	11.64	17.77	34.57	53.58
		6.20	11.03	19.06	36.66	60.39
		6.64	11.79	18.73	37.00	55.86
		6.50	11.77	18.13	35.73	57.64
	F	6.32	11.73	17.07	35.57	54.17
		6.04	11.59	18.28	35.78	54.32
		6.04	10.68	18.00	33.86	52.40
		6.25	10.81			
		6.18	10.80			
		6.74	10.77			
		6.91	10.16			
66	M	7.06	11.66	17.08	37.84	56.72
		6.51	10.64	19.64	35.18	61.91
		7.07	12.63	17.61	35.48	56.61
		6.42	12.08	17.73	35.09	62.11
		6.09	11.10	18.72	35.89	61.28
		6.63	10.93	18.24	35.01	65.27
	F	6.08	11.80	18.76	34.79	59.35
		6.17	11.02	19.01	36.61	59.93
		6.07	10.41	17.58	35.11	59.82
		5.57	12.08	18.84	35.79	57.86
		6.18	11.47			
		6.78	10.64			
		7.22	9.49			
68	M	6.35	11.16	18.12	34.50	60.11
		6.13	9.93	17.60	36.89	60.57
		6.33	10.25	17.63	36.61	56.02
		6.40	11.00	18.24	34.44	59.60
		6.55	10.67	17.01	35.41	58.76
		6.31	10.31	17.51	35.89	58.32
		6.73	10.56	17.28	35.68	57.66
		6.52	10.22	16.98	34.92	58.57
	F	6.11	10.07	17.27	35.65	60.13
		5.98	10.59	18.03	35.70	56.93
		6.58	10.87			
		6.24	10.07			
		5.88	10.95			
		6.16	9.84			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 11 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
70	M	5.92	9.96	12.69	30.69	49.25
		5.77	9.47	16.04	31.75	43.70
		5.74	8.96	14.51	30.51	52.25
		6.03	9.55	15.53	30.94	50.62
		6.02	8.41	15.20	31.40	50.71
		6.24	9.23	15.08	26.61	47.66
	F	5.69	9.33	14.59	31.73	41.01
		5.89	9.26	14.30	29.18	51.17
		5.61	8.16	14.81	25.36	49.44
		5.48	6.33	10.25	30.99	48.05
		5.85	8.84			
		4.87	9.36			
		5.51	9.06			
		5.39	8.57			
		6.00	9.19			
72	M	7.41	13.19	21.07	38.41	61.78
		7.40	13.17	22.22	36.60	66.85
		7.72	13.34	21.25	35.97	61.50
		7.69	13.53	20.34	37.60	63.24
		7.60	13.88	21.20	37.96	62.80
		7.48	13.47	21.16	38.22	60.92
		7.38	13.00	20.60	39.14	60.70
		7.47	13.04	20.44	36.83	60.65
	F	6.74	12.33	20.28	39.01	62.48
		7.22	13.12	21.22	37.77	59.77
		7.15	12.96			
		7.60	11.88			
74	M	6.89	9.59	17.74	33.72	62.70
		6.56	9.19	16.50	38.46	57.86
		6.31	10.72	18.36	36.91	63.75
		6.21	11.48	18.45	36.04	61.00
		6.44	9.82	14.74	34.36	63.67
		5.10	10.68	16.10	34.10	55.23
		6.81				
	F	6.21	9.75	16.86	33.89	53.63
		5.82	10.21	15.68	33.67	55.70
		5.79	9.33	13.07	33.85	50.31
		6.10	10.26	15.46	31.43	55.83
		5.91	9.29			
		5.94	9.90			
		6.46	9.21			
		.[h]	7.54			
		.[d]	9.25			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 12 of 16)

Female ID	Sex	Postnatal Day				
		0	4	7	14	21
76	M	5.82	9.09	15.76	34.01	53.50
		5.65	10.00	15.92	33.33	59.29
		6.04	9.36	16.14	34.24	58.84
		6.18	9.78	15.02	33.66	57.07
		5.29	9.54	14.64	34.08	56.10
		5.86	9.70	16.15	32.34	56.79
		5.93	8.84	16.20	31.09	56.31
		6.15				
	F	5.58	9.34	14.75	31.07	55.16
		5.46	8.19	15.03	30.72	51.89
		5.17	9.33	15.35	32.47	54.70
		5.54	9.59			
		5.64	9.29			
		.[d]	9.07			
78	M	6.76	11.35	16.33	33.87	61.73
		7.21	11.01	18.07	35.73	62.30
		6.94	11.84	18.41	34.47	63.34
		7.08	11.64	16.77	34.86	59.49
		6.23	10.96	17.80	33.70	57.43
		7.10	10.17	15.91	33.92	57.35
	F	6.24	9.57	15.23	29.73	53.46
		6.61	11.17	13.34	30.72	59.16
		6.55	10.01	16.89	32.62	54.97
		6.51	10.61	17.38	34.99	50.94
		5.88	10.78			
80	M	5.96	9.76	16.42	36.90	55.34
		5.64	9.00	16.17	33.66	56.81
		6.33	9.49	17.30	34.21	52.72
		6.32	9.43	16.57	33.95	57.39
		6.22	8.77	15.57	31.04	58.16
		6.18	9.82	17.37	31.90	60.56
		6.47	9.15	15.01	35.27	59.43
		5.87	10.05	15.32	33.27	58.56
		5.96	9.60	15.79	32.12	62.72
	F	6.05	9.95	16.46	34.09	57.14
		6.29	10.01			
		5.91	10.27			
		6.43	9.57			
		5.95	9.95			
		6.28	9.77			
		6.16	9.25			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 13 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
82	M	6.52	11.49	18.09	34.14	58.29
		6.42	12.04	17.41	35.89	57.61
		6.89	10.61	17.64	35.41	57.32
		6.68	11.44	18.92	34.12	59.88
		6.92	11.32	18.30	34.50	58.78
		7.35	11.53	18.22	34.09	55.90
	F	6.78	11.26	17.01	32.72	58.14
		6.73	11.11	17.85	34.46	55.22
		6.42	11.14	17.36	34.05	55.40
		6.68	10.56	17.17	33.95	57.06
		6.14	10.85			
		6.84	11.39			
84	M	6.70	10.85	11.00	36.11	58.73
		5.92	10.54	17.85	35.77	59.00
		6.27	11.06	17.92	36.52	28.10
		6.64	10.98	18.14	35.44	58.68
		6.34	10.71	17.84	34.22	58.17
		6.41	7.53	17.86	22.04	59.86
		6.27	11.04	18.03	35.98	57.40
		6.39	11.52	17.43	34.99	58.13
	F	5.58	11.36	18.42	35.76	58.99
		6.51	9.88	18.56	36.71	57.85
		5.12	11.44			
		6.15	9.94			
		6.14	10.50			
		6.61	.[e]			
86	M	7.22	12.32	17.52	34.71	62.26
		7.35	12.03	17.91	32.68	55.74
		7.09	12.16	17.97	33.68	55.75
		7.08	12.07	17.61	36.11	56.18
	F	6.11	10.98	17.00	32.76	54.67
		6.28	11.17	16.46	33.11	55.15
		6.14	11.54	15.53	32.97	55.52
		6.26	11.28	16.71	32.01	53.54
		6.82	11.43	16.63	32.38	49.03
		6.57	9.98	17.66	30.55	53.04
		6.80	11.15			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 14 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
88	M	6.46	10.33	17.61	34.36	52.95
		6.36	9.59	15.54	33.14	55.14
		6.20	10.65	16.51	31.99	49.80
		6.31	10.58	15.20	31.14	49.04
		6.50	10.16	15.98	33.12	50.79
		5.91	9.53	16.94	31.30	52.59
		6.54	10.36	16.73	32.58	50.10
		6.18	10.25	16.88	29.32	48.12
	F	5.77	9.99	15.88	30.27	45.59
		6.30	9.46	15.82	31.50	48.62
		5.79	9.38			
		6.02	9.63			
		5.90	10.46			
90	M	6.33	9.55	12.85	26.90	48.48
		5.21	9.86	14.85	30.73	51.34
		6.26	8.25	15.78	31.18	50.39
		6.47	9.99	15.80	32.20	44.23
	F	5.55	9.41	13.83	30.63	47.78
		6.25	9.79	13.64	28.94	49.07
		5.55	9.21	14.28	29.43	37.27
		4.85	8.68	15.39	29.24	48.98
		5.94	6.24	15.03	23.00	49.47
		5.92	9.15	9.79	30.39	46.84
		6.11	8.80			
		5.74	8.87			
		5.59	9.40			
92	M	6.20	10.24	15.78	28.51	51.09
		5.55	9.87	14.46	28.88	48.04
		5.74	9.72	15.09	30.12	43.18
		5.89	9.13	15.27	29.11	46.70
		6.23	9.33	14.33	28.05	46.10
	F	5.68	9.12	14.04	28.18	45.03
		5.63	9.46	14.25	26.67	47.71
		5.51	9.66	14.90	29.10	46.47
		5.78	9.27	14.61	27.63	42.69
		5.75	8.87	14.18	27.31	47.82
		5.63	8.96			
		5.77	9.34			
		5.81	9.56			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 15 of 16)

Female ID	Sex	Postnatal Day 0	4	7	14	21
94	M	5.97	9.78	14.74	31.46	46.57
		6.10	9.21	14.86	29.68	48.02
		6.20	9.16	14.71	30.05	46.08
		6.33	9.81	15.81	31.34	49.33
		6.03	9.48	14.49	31.84	45.58
		6.64	9.95	14.68	29.27	45.41
		6.15	9.76	15.74	30.34	48.70
		6.64	9.19	14.47	29.57	48.42
		6.55	9.17	15.23	30.56	46.97
		6.45				
		6.30	.[e]			
	F	5.98	9.07	14.28	30.81	46.58
		6.34	9.58			
		6.50	8.44			
		6.15	10.19			
		5.77	9.24			
		.[d]	8.93			
96	M	7.43	12.99	20.70	40.12	63.59
		7.38	12.28	19.36	40.53	62.43
		6.58	12.12	19.27	38.89	66.62
		7.07	12.52	19.10	40.20	56.75
		7.01	11.89	20.33	40.10	64.13
		6.86	12.78	19.31	37.90	63.65
	F	6.97	12.91	20.95	38.75	63.32
		6.95	12.42	18.82	38.03	59.95
		7.34	12.37	20.59	39.98	62.33
		7.04	12.79	19.49	38.08	63.25
		7.44	13.04			
98	M	6.24	11.18	16.26	31.15	54.36
		6.76	9.90	18.01	33.90	55.08
		6.98	11.27	19.00	35.85	49.83
		6.37	11.21	18.17	32.16	57.01
		6.78				
		6.75				
	F	6.41	11.10	18.69	34.39	50.41
		6.60	10.62	16.45	32.58	52.72
		6.82	11.61	17.58	30.61	51.27
		4.78	10.60	17.77	32.72	48.37
		6.14	11.24	17.08	33.28	51.09
		6.54	10.04	17.22	31.59	51.06
		6.15	10.46			
		7.07	11.40			
		5.97	11.14			
		.[d]	8.78			
		.[d]	6.36			

(continued)

Table B-6. Individual Body Weight (g) during Lactation for the F_1 Pups from the F_0 Untreated Females[a]
(page 16 of 16)

Female ID	Sex	Postnatal Day				
		0	4	7	14	21
100	M	7.11	11.25	19.35	39.82	61.92
		7.67	11.90	18.01	38.32	62.77
		7.04	11.34	17.65	37.85	64.22
		.[d]	12.52	18.26	38.17	62.74
	F	7.15	9.74	9.88	34.92	57.75
		6.72	11.05	16.90	37.40	54.54
		6.66	7.01	15.77	27.25	60.08
		4.60	11.03	16.66	35.81	43.77
		7.26				

[a]Pup body weights are not comparable across columns because the pups were not uniquely identified until postnatal day 21. Litters were culled to 10 pups (maximum number of males) on postnatal day 4
[b]Females 2 through 50 were in component 1 and females 52 through 100 were in component 2.
[c]Female was removed from the study because her correct postnatal day 0 could not be confirmed.
[d]Pup was missexed.
[e]Pup missing and presumed dead on postnatal day 4.
[f]Pup was culled on postnatal day 4 due to a physical malformation.
[g]Pup was found dead on postnatal day 21.
[h]Body weight was inadvertently not recorded.

Table B-7. Individual Clinical Observations during Lactation for the F_1 Pups from the F_0 Untreated Females (page 1 of 1)

Female ID	Day	Sex	Clinical Observation
8[a]	0	M	No milk band
16	0	M	Found dead
18	4	M	Missing and presumed dead
22	0	F	Found dead
	14	F	Eye(s): not open
	21	F	Eye(s): not open; Head: domed
26	4	F	Missing and presumed dead
28	0	F	Found dead
30	0	F	Found dead
	4	M	Tail: thread-like; Pup culled
40	0	F	Found dead
		M	Found dead
			Found dead
	14	F	Thin fur: back
			Thin fur: back
			Thin fur: back
		M	Thin fur: back
			Thin fur: back
			Thin fur: back
46	21	F	Cannibalized, 1 x 2 cm piece of fur/skin only
56	4	M	Missing and presumed dead
60	4	M	Missing and presumed dead
64	14	M	Tail: kinked
84	4	F	Missing and presumed dead
94	4	M	Missing and presumed dead

[a]Females 2 through 50 were in component 1 and females 52 through 100 were in component 2.

Table B-8. Individual Necropsy Findings during Lactation for the F_1 Pups from the F_0 Untreated Females
(page 1 of 1)

Female ID	Day	Sex	Necropsy Finding
16	0	M	Ductus open; Milk in stomach
22	0	F	Necropsy inadvertently not performed
28	0	F	Ductus open; Digestive tract too autolyzed to evaluate
30	0	F	Ductus open; No air in lungs; No milk in stomach
40	0	F	Ductus open; No air in lungs; No milk in stomach
		M	Ductus open; No air in lungs; No milk in stomach
			Placenta still attached; Ductus open; No air in lungs; No milk in stomach
46	21	F	Cannibalized, unable to evaluate

[a]Females 2 through 50 were in component 1 and females 52 through 100 were in component 2.

FINAL REPORT
APPENDICES II - V

Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 to 52/53

Authors:

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Sponsor's Representative:

David P. Houchens, Ph.D.
EDSP Program Manager
Battelle

Study Initiation Date:

May 20, 2002

In-Life Performance Dates:

September 5, 2002 - November 7, 2002
(Component 1)

December 26, 2002 - February 26, 2003
(Component 2)

Experimental Dates:

October 7, 2002 - October 22, 2003
January 26, 2003 - October 22, 2003

Final Report Date:

February 9, 2004

RTI Identification Number:

08055.001.015.001

Appendix II

Histopathology Report

- Corrected pages with transmittal letter dated January 22, 2004
- Pathology report (October 22, 2003), Experimental Laboratories, Inc.

EPL®

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.
P.O. BOX 12766, RESEARCH TRIANGLE PARK, NC 27709 (919)998-9407 Fax: (919)998-9607

January 22, 2004

Dr. Julia George
Senior Toxicologist
Research Triangle Institute
P.O. Box 12194
Research Triangle Park, NC 27709-2194

Dear Dr. George:

Please find an original and one punched copy of page 2 and the leader pages for the two components from the final pathology report entitled "Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 Through 52/53" – Client ID 65U-08055.001.015.001(M) – EPL Project No. 237-006.

If there are any questions regarding these pages, please do not hesitate to contact me.

Sincerely,

John Curtis Seely, DVM

JOHN CURTIS SEELY, ~~D.V.~~M.
Diplomate ACVP
Senior Pathologist

JCS:amh

Enclosures

DESIGN OF THE STUDY

Eight test chemicals were administered via gavage once daily for 31-32 consecutive days (pnd 22 to pnd 52 or 53) to male CD® (Sprague-Dawley) rats under the study conditions outlined in the study protocol (RTI Master Protocol No.: RTI-831).

The study began with 15 weight-matched F1 males/group. The study design, test chemicals and target dose levels are presented in Table 1.

Table 1 – Study Design

Component 1

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Methoxychlor	25	5.0	5.0
3	15		50	10.0	5.0
4	15	Atrazine	75	15.0	5.0
5	15		150	30.0	5.0
6	15	p,p-DDE	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Vinclozolin	30	6.0	5.0
9	15		100	20.0	5.0

[a] corn oil, vehicle control

Component 2

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Propylthiouracil	2	0.4	5.0
3	15		25	5.0	5.0
4	15	Linuron	50	10.0	5.0
5	15		100	20.0	5.0
6	15	Ketoconazole	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Phenobarbital	50	10.0	5.0
9	15		100	20.0	5.0

[a] corn oil, vehicle control

Study Design

Component 1

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Methoxychlor	25	5.0	5.0
3	15		50	10.0	5.0
4	15	Atrazine	75	15.0	5.0
5	15		150	30.0	5.0
6	15	p,p-DDE	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Vinclozolinp	30	6.0	5.0
9	15		100	20.0	5.0

[a] corn oil, vehicle control

Study Design

Component 2

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Propylthiouracil	2	0.4	5.0
3	15		25	5.0	5.0
4	15	Linuron	50	10.0	5.0
5	15		100	20.0	5.0
6	15	Ketoconazole	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Phenobarbital	50	10.0	5.0
9	15		100	20.0	5.0

[a] corn oil, vehicle control

ASSESSMENT OF PUBERTAL DEVELOPMENT AND THYROID FUNCTION IN JUVENILE MALE CD® (SPRAGUE-DAWLEY) RATS AFTER EXPOSURE TO SELECTED CHEMICALS ADMINISTERED BY GAVAGE ON POSTNATAL DAYS 23 THROUGH 52/53

65U-08055.001.015.001(M)

EPL PROJECT NO. 237-006

PATHOLOGY REPORT

Submitted to

Research Triangle Institute
P.O. Box 12194
Research Triangle Park, NC 27709

Submitted by

Experimental Pathology Laboratories, Inc.
P.O. Box 12766
Research Triangle Park, NC 27709

October 22, 2003

TABLE OF CONTENTS

ASSESSMENT OF PUBERTAL DEVELOPMENT AND THYROID FUNCTION IN JUVENILE MALE CD® (SPRAGUE-DAWLEY) RATS AFTER EXPOSURE TO SELECTED CHEMICALS ADMINISTERED BY GAVAGE ON POSTNATAL DAYS 23 THROUGH 52/53

65U-08055.001.015.001(M)

EPL PROJECT NO. 237-006

NARRATIVE SUMMARY

INTRODUCTION

The objective of this study was to quantify the effects of environmental compounds on pubertal development and thyroid function in the intact juvenile/peripubertal male rat. This assay detects compounds that display antithyroid, estrogenic, androgenic, antiandrogenic [androgen receptor (AR) or steroid enzyme mediated] activity, or alter follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, growth hormone (GH), or hypothalamic function.

For this study, the following chemicals were tested: Methoxychlor, Atrazine, p-p-DDE, Vinclozolin, Propylthiouracil, Linuron, Ketoconazole, and Phenobarbital. The study was conducted in two components. Each component consisted of two dose groups per test material and one vehicle control group, each group comprised of 15 weight-matched F1 male weanlings, for each of the two components.

The testes, epididymides and thyroids were examined microscopically.

SUMMARY

Administration of the test chemicals by gavage to male, CD® (Sprague-Dawley) rats, under the conditions of this study, was associated with the following histopathologic changes:

1. The presence and dose-related increased severity of thyroid, follicular cell hypertrophy/hyperplasia in both the 2 and 25 mg/kg dosed Propylthiouracil animals.

DESIGN OF THE STUDY

Eight test chemicals were administered via gavage once daily for 31-32 consecutive days (pnd 22 to pnd 52 or 53) to male CD® (Sprague-Dawley) rats under the study conditions outlined in the study protocol (RTI Master Protocol No.: RTI-831).

The study began with 15 weight-matched F1 males/group. The study design, test chemicals and target dose levels are presented in Table 1.

Table 1 – Study Design

Component 1

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Methoxychlor	25	5.0	5.0
3	15		50	10.0	5.0
4	15	Atrazine	75	15.0	5.0
5	15		150	30.0	5.0
6	15	p,p-DDE	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Vinclozolin	30	6.0	5.0
9	15		100	20.0	5.0

[a] stripped corn oil, vehicle control

Component 2

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Propylthiouracil	2	0.4	5.0
3	15		25	5.0	5.0
4	15	Linuron	50	10.0	5.0
5	15		100	20.0	5.0
6	15	Ketoconazole	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Phenobarbital	50	10.0	5.0
9	15		100	20.0	5.0

[a] stripped corn oil, vehicle control

Individual treatment groups within each component of the study were given unique five digit codes that are presented in Table 2.

Table 2 – Treatment Group Designations

Group	Component 1	Component 2
1	78967	82703
2	96509	04691
3	68843	65437
4	84156	46916
5	39239	59969
6	29505	27489
7	48266	16317
8	15492	34563
9	07983	95962

According to the study protocol, all F1 males were subjected to a complete necropsy with selected organs dissected and weighed. The testes and epididymides were fixed in Bouin's fixative for 24 hours, after which they were rinsed and stored in 70% alcohol. The thyroid with attached portion of trachea was fixed in 10% buffered neutral formalin. All tissues were trimmed, embedded in paraffin, sectioned and stained with Hematoxylin and Eosin (H&E).

Histopathological examination of selected organs was conducted on the protocol-required tissues. The protocol-required tissues were: testis, epididymis and thyroid glands.

The gross and histopathologic data were entered in the Experimental Pathology Laboratories, Inc. Computerized Pathology Reporting System. Each lesion was graded according to a four-grade severity scale (1-4). "Aspermia" of the epididymis was designated only as "Present".

RESULTS

The individual animal data are presented by group in the Histopathology Incidence Table (HIT) and the group summary data in the Summary Incidence Tables (SIT). Gross necropsy findings were correlated to the microscopic findings, whenever possible. These findings are presented in the section "Correlation of Gross and Microscopic Findings Tables".

A limited number of histopathologic changes were observed during the study. No lesions were noted in any control animals from either Component 1 or Component 2. A few degenerative lesions of the testicular seminiferous tubules associated, in some cases, with the presence of exfoliated germ cells in epididymal tubule lumens were occasionally observed. None of these changes appeared to be treatment-related because of their overall low incidence and lack of any dose response.

In addition, because of the young age of the animals, the epididymal tubules appeared to be slightly immature and fewer sperm compared to older animals were present. This was particularly noted in the epididymal cauda of all animals examined.

The following chemicals were not associated with any treatment-related histopathologic changes: Component 1 = Methoxychlor (25 and 50 mg/kg); Atrazine (75 and 150 mg/kg), p,p-DDE (50 and 100 mg/kg), and Vinclozolin (30 and 100 mg/kg); Component 2 = Linuron (50 and 100 mg/kg), Ketoconazole (50 and 100 mg/kg), and Phenobarbital (50 and 100 mg/kg).

Although some relative and/or adjusted organ weight changes were statistically different (either increased or decreased) for the testes, epididymides or thyroid glands for several of the above chemicals, no related histopathology by routine H&E examination was detected in these tissues to account for the weight changes.

TREATMENT-RELATED FINDINGS BY CHEMICAL

Propylthiouracil

Administration of both 2 and 25 mg/kg Propylthiouracil was associated with the presence and dose-related increased severity of thyroid follicular cell hypertrophy/hyperplasia which was clearly related to increased thyroid weights and levels of TSH and decreased levels of T4.

Follicular cell hypertrophy/hyperplasia was characterized by a spectrum of histologic changes including the increased size and apparent number of follicular cells, the reduction in follicular lumen size, the presence of thyroid follicles. The severity of hypertrophy/hyperplasia was subjectively based on a

number of criteria: minimal = multifocal follicles affected, size and number of follicular cells slightly enlarged and increased; mild = diffuse change with further increased cell size and hyperplasia; moderate = enhanced severity with the presence of notable numbers of follicular cell mitoses; marked = increased mitotic rate, some degenerative cells (deeply eosinophilic cytoplasm and pyknotic nuclei) within the follicular epithelium, and obvious thyroid gland size and shape enlargement. No alteration of the thyroid vasculature was noted.

The incidence and severity of thyroid hypertrophy/hyperplasia is presented in Table 3.

Table 3 – Incidence and Severity of Thyroid Hypertrophy/Hyperplasia
Propylthiouracil

Dose (mg/kg)	0	2	25
THYROID (No. Examined)	(14)	(15)	(14)
Hypertrophy/Hyperplasia	0	15	14
Mild	0	10	1
Moderate	0	5	9
Marked	0	0	4

Results of the microscopic examination of the thyroid gland are compatible with previous reports on the direct action of Propylthiouracil on the thyroid gland (Thomas and Williams, 1999).

John Curtis Seely, DVM

JOHN CURTIS SEELY, D.V.M.
Diplomate, ACVP
Senior Pathologist

October 22, 2003
Date

REFERENCES

Thomas GA and Williams ED. Thyroid Stimulating Hormone (TSH) – Associated Follicular Hypertrophy and Hyperplasia as a Mechanism of Thyroid Carcinogenesis in Mice and Rats. In. Species Differences in Thyroid, Kidney, and Urinary Bladder Carcinogenesis. Capen CC, Dybing E, Rice JM, and Wilbourn (Eds) IARC Scientific Publications No. 147, pp 45-59, 1999.

EXPERIMENTAL PATHOLOGY LABORATORIES, INC.

QUALITY ASSURANCE FINAL CERTIFICATION

Study Title: Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 Through 52/53

Client Study: RTI Contract 65U-08055.001.015.001(M) EPL Project Coordinator: Dr. John Curtis Seely

EPL Project Number: 237-006 EPL Pathologist: Dr. John Curtis Seely

The following aspects of this study were inspected by the Quality Assurance Unit of Experimental Pathology Laboratories, Inc. Dates inspections were performed and findings reported to the EPL Project Coordinator and Management are indicated below.

	Dates	
Area Inspected	Inspection	Reporting
EPL Project Sheets	October 8, 2002; December 13, 2002; March 10, 2003	October 8, 2002; December 13, 2002; March 10, 2003
Project Setup	November 26&27, 2002; March 11, 2003	November 27, 2002; March 11, 2003
Histology Setup	November 27, 2002; March 12, 2003	November 27, 2002; March 12, 2003
Data Review	January 17, 2003; April 11, 2003	January 17, 2003; April 11, 2003
Draft Report	July 2&3, 2003	July 3, 2003
Final Report	October 22, 2003	October 22, 2003

Date Reported to Study Director/Management: October 22, 2003

Date of last quarterly facility inspection: August 2003

Jane J. Hollingsworth
EPL Quality Assurance Unit

October 22, 2003
Date

Form No. 6-2 (09/10/99)

Study Design

Component 1

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Methoxychlor	25	5.0	5.0
3	15		50	10.0	5.0
4	15	Atrazine	75	15.0	5.0
5	15		150	30.0	5.0
6	15	p,p-DDE	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Vinclozolin	30	6.0	5.0
9	15		100	20.0	5.0

[a] stripped corn oil, vehicle control

SUMMARY INCIDENCE TABLES

COMPONENT #1

SUMMARY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 6
EPIDIDYMIS (NO. EXAMINED)	(12)	(15)	(13)	(12)	(12)	(13)
Aspermia				1		
Exfoliated Germ Cells, Lumen				1		
TESTIS (NO. EXAMINED)	(12)	(15)	(13)	(12)	(12)	(13)
Degeneration, Seminiferous						
Tubule				1		
THYROID (NO. EXAMINED)	(12)	(15)	(13)	(12)	(12)	(13)

SUMMARY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

	GROUP 7	GROUP 8	GROUP 9			
EPIDIDYMIS (NO. EXAMINED)	(15)	(13)	(12)			
Aspermia						
Exfoliated Germ Cells, Lumen						
TESTIS (NO. EXAMINED)	(15)	(13)	(12)			
Degeneration, Seminiferous						
Tubule		1				
THYROID (NO. EXAMINED)	(15)	(13)	(12)			

HISTOPATHOLOGY INCIDENCE TABLES

COMPONENT #1

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

GROUP 1

ANIMAL	1	15	32	33	50	51	68	87	104	105	122	123								
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X								
Aspermia																				
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X								
Degeneration, Seminiferous Tubule																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X								

EPL
Experimental Pathology Laboratories, Inc.

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

	GROUP 2																			
ANIMAL	2	16	31	34	49	52	67	70	85	88	103	106	121	124	134					
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Aspermia																				
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Degeneration, Seminiferous Tubule																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

	GROUP 3												
ANIMAL	3	14	35	48	53	66	71	84	89	102	107	120	125
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X
Aspermia													
Exfoliated Germ Cells, Lumen													
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X
Degeneration, Seminiferous Tubule													
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X

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HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

GROUP 4

ANIMAL	4	29	36	47	65	72	83	90	101	108	126	133
EPIDIDYMIS	X	X	X	X	X	X	X	X		X	X	X
Aspermia									P			
Exfoliated Germ Cells, Lumen									3			
TESTIS	X	X	X	X	X	X	X	X		X	X	X
Degeneration, Seminiferous Tubule									3			
THYROID	X	X	X	X	X	X	X	X	X	X	X	X

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

GROUP
5

ANIMAL	5	13	19	28	37	46	64	73	82	91	100	109								
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X								
Aspermia																				
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X								
Degeneration, Seminiferous Tubule																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X								

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P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

	GROUP 6																			
ANIMAL	6	12	27	38	45	56	63	81	92	99	110	117	128							
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X							
Aspermia																				
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X							
Degeneration, Seminiferous Tubule																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X							

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1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

GROUP 7

ANIMAL	7	21	26	39	44	57	62	75	80	93	98	111	116	129	132					
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Aspermia																				
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Degeneration, Seminiferous Tubule																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					

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Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

GROUP 8

ANIMAL	8	11	22	25	40	43	58	61	76	94	97	112	130
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X
Aspermia													
Exfoliated Germ Cells, Lumen													
TESTIS	X	X	X		X	X	X	X	X	X	X	X	X
Degeneration, Seminiferous Tubule				1									
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X

EPL
Experimental Pathology Laboratories, Inc.

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
F1 Sacrifice
Male Rat

GROUP 9

ANIMAL	9	10	23	41	42	59	60	77	78	95	96	113								
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X								
Aspermia																				
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X								
Degeneration, Seminiferous Tubule																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X								

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS TABLES

COMPONENT #1

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 1

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
15	KIDNEY	Right side, hydronephrosis	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 3

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
89	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 4

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
101	TESTIS	Left, not descended	No Comment Required
	TESTIS	Left, smaller in size	Degeneration, Seminiferous Tubule
	EPIDIDYMIS	Left, smaller in size	Exfoliated Germ Cells, Lumen; Aspermia
133	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 5

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
13	KIDNEY	Right, hydronephrosis, mild	Intentionally Not Sampled
91	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled

08055.001
F1 Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 6

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
12	KIDNEY	Right side, hydronephrosis, slight	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 7

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
7	NOSE	Chromodacryorrhea (not saved)	Intentionally Not Sampled
26	INTESTINES	Distended with air	Intentionally Not Sampled
39	KIDNEY	Bilateral, hydronephrosis	Intentionally Not Sampled
44	KIDNEY	Right side, hydronephrosis, slight	Intentionally Not Sampled
98	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
116	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 8

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
8	KIDNEY	Right side, hydronephrosis	Intentionally Not Sampled
11	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
22	KIDNEY	Right side, hydronephrosis	Intentionally Not Sampled
61	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 9

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
10	KIDNEY	Right side, hydronephrosis	Intentionally Not Sampled
42	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
59	KIDNEY	Right side, hydronephrosis	Intentionally Not Sampled
	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled

Study Design

Component 2

Group No.	No. F1 Males	Chemical	Dose mg/kg/day	Concentration mg/ml	Dose Volume ml/kg
1	15	-[a]	0	0.0	5.0
2	15	Propylthiouracil	2	0.4	5.0
3	15		25	5.0	5.0
4	15	Linuron	50	10.0	5.0
5	15		100	20.0	5.0
6	15	Ketoconazole	50	10.0	5.0
7	15		100	20.0	5.0
8	15	Phenobarbital	50	10.0	5.0
9	15		100	20.0	5.0

[a] stripped corn oil, vehicle control

SUMMARY INCIDENCE TABLES

COMPONENT #2

SUMMARY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 6
EPIDIDYMIS (NO. EXAMINED)	(14)	(15)	(14)	(15)	(15)	(15)
Exfoliated Germ Cells, Lumen						1
TESTIS (NO. EXAMINED)	(14)	(15)	(14)	(15)	(15)	(15)
Degeneration, Seminiferous Tubule			1			1
THYROID (NO. EXAMINED)	(14)	(15)	(14)	(15)	(15)	(15)
Congestion		1				
Hemorrhage, Follicle						
Hypertrophy/Hyperplasia, Follicular Cell		15	14			

SUMMARY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

	GROUP 7	GROUP 8	GROUP 9			
EPIDIDYMIS (NO. EXAMINED)	(14)	(15)	(15)			
Exfoliated Germ Cells, Lumen			1			
TESTIS (NO. EXAMINED)	(14)	(15)	(15)			
Degeneration, Seminiferous Tubule						
THYROID (NO. EXAMINED)	(14)	(15)	(15)			
Congestion						
Hemorrhage, Follicle			1			
Hypertrophy/Hyperplasia, Follicular Cell						

HISTOPATHOLOGY INCIDENCE TABLES

COMPONENT #2

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

GROUP 1

	ANIMAL	136	153	154	171	172	182	199	200	218	235	236	253	254	270						
EPIDIDYMIS		X	X	X	X	X	X	X	X	X	X	X	X	X	X						
Exfoliated Germ Cells, Lumen																					
TESTIS		X	X	X	X	X	X	X	X	X	X	X	X	X	X						
Degeneration, Seminiferous Tubule																					
THYROID		X	X	X	X	X	X	X	X	X	X	X	X	X	X						
Congestion																					
Hemorrhage, Follicle																					
Hypertrophy/Hyperplasia, Follicular Cell																					

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
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m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

	GROUP 2																			
ANIMAL	137	152	155	170	173	183	198	201	216	219	234	237	252	255	269					
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Degeneration, Seminiferous Tubule																				
THYROID																				
Congestion			2																	
Hemorrhage, Follicle																				
Hypertrophy/Hyperplasia, Follicular Cell	2	3	2	3	3	2	3	2	3	2	2	2	2	2	2					

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

GROUP 3

ANIMAL	138	151	156	169	174	184	197	202	215	220	233	238	251	256						
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X						
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X		X	X	X						
Degeneration, Seminiferous																				
Tubule											1									
THYROID																				
Congestion																				
Hemorrhage, Follicle																				
Hypertrophy/Hyperplasia,																				
Follicular Cell	4	2	3	4	3	4	3	3	3	3	4	3	3	3						

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P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

	GROUP 4														
ANIMAL	139	150	157	168	175	185	196	203	214	221	232	239	250	257	267
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Exfoliated Germ Cells, Lumen															
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Degeneration, Seminiferous Tubule															
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Congestion															
Hemorrhage, Follicle															
Hypertrophy/Hyperplasia, Follicular Cell															

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
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HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

GROUP
5

ANIMAL	140	149	158	167	176	186	195	204	213	222	231	240	249	258	266					
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Exfoliated Germ Cells, Lumen																				
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Degeneration, Seminiferous Tubule																				
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Congestion																				
Hemorrhage, Follicle																				
Hypertrophy/Hyperplasia, Follicular Cell																				

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Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

GROUP 6

ANIMAL	141	148	159	166	177	187	194	205	212	223	230	241	248	259	265					
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X						
Exfoliated Germ Cells, Lumen															2					
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X						
Degeneration, Seminiferous Tubule															1					
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X					
Congestion																				
Hemorrhage, Follicle																				
Hypertrophy/Hyperplasia, Follicular Cell																				

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

GROUP
7

ANIMAL	142	147	160	165	178	188	193	206	211	224	229	247	260	264
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Exfoliated Germ Cells, Lumen														
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Degeneration, Seminiferous Tubule														
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Congestion														
Hemorrhage, Follicle														
Hypertrophy/Hyperplasia, Follicular Cell														

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

	GROUP 8																		
ANIMAL	143	146	161	164	179	189	192	207	210	225	228	243	246	261	263				
EPIDIDYMIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Exfoliated Germ Cells, Lumen																			
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Degeneration, Seminiferous Tubule																			
THYROID	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Congestion																			
Hemorrhage, Follicle																			
Hypertrophy/Hyperplasia, Follicular Cell																			

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

HISTOPATHOLOGY INCIDENCE TABLE

08055.001
Terminal Sacrifice
Male Rat

	GROUP 9																		
ANIMAL	144	145	162	163	180	181	190	191	208	209	226	227	244	245	262				
EPIDIDYMIS	X	X	X	X	X	X		X	X	X	X	X	X	X	X				
Exfoliated Germ Cells, Lumen							1												
TESTIS	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X				
Degeneration, Seminiferous Tubule																			
THYROID	X		X	X	X	X	X	X	X	X	X	X	X	X	X				
Congestion																			
Hemorrhage, Follicle		1																	
Hypertrophy/Hyperplasia, Follicular Cell																			

Key : X=Not Remarkable N=No Section I=Incomplete A=Autolysis
1=minimal 2=mild 3=moderate 4=severe
P=Present B=Benign M=Malignant
m=missing one paired organ u=unscheduled sac./death

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS TABLES

COMPONENT #2

08055.001
Terminal Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 1

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
199	URINARY BLADDER	Multiple 1-3mm calculi	Intentionally Not Sampled
	URINARY BLADDER	Wall, thickened	Intentionally Not Sampled

08055.001
Terminal Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 2

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
152	THYROID	Left side, enlarged and darkened	Hypertrophy/Hyperplasia, Follicular Cell
170	THYROID	Slightly enlarged and darkened	Hypertrophy/Hyperplasia, Follicular Cell
173	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
	THYROID	Right side, slightly enlarged	Hypertrophy/Hyperplasia, Follicular Cell
	THYROID	Darkened	Hypertrophy/Hyperplasia, Follicular Cell
183	THYROID	Increased in size	Hypertrophy/Hyperplasia, Follicular Cell
198	THYROID	Enlarged, bilateral	Hypertrophy/Hyperplasia, Follicular Cell
201	THYROID	Increased in size	Hypertrophy/Hyperplasia, Follicular Cell
219	PROSTATE	Ventral and dorsolateral, reduced in size	Intentionally Not Sampled
	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
	THYROID	Enlarged and reddened, bilateral	Hypertrophy/Hyperplasia, Follicular Cell
237	THYROID	Enlarged and reddened	Hypertrophy/Hyperplasia, Follicular Cell
252	THYROID	Enlarged	Hypertrophy/Hyperplasia, Follicular Cell
269	LUNG	Multiple foci	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 3

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
138	THYROID	Increased in size	Hypertrophy/Hyperplasia, Follicular Cell
151	THYROID	Enlarged, bilaterally	Hypertrophy/Hyperplasia, Follicular Cell
156	THYROID	Enlarged and red, bilaterally	Hypertrophy/Hyperplasia, Follicular Cell
169	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
	THYROID	Enlarged/reddened, bilateral	Hypertrophy/Hyperplasia, Follicular Cell
174	LIVER	Reduced in size	Intentionally Not Sampled
	THYROID	Enlarged and reddened, bilateral	Hypertrophy/Hyperplasia, Follicular Cell
184	THYROID	Enlarged and reddened, bilateral	Hypertrophy/Hyperplasia, Follicular Cell
197	LIVER	Appears mottled	Intentionally Not Sampled
	THYROID	Enlarged	Hypertrophy/Hyperplasia, Follicular Cell
202	THYROID	Enlarged and reddened, bilateral	Hypertrophy/Hyperplasia, Follicular Cell
	PITUITARY	Reduced in size	Intentionally Not Sampled
215	ADRENAL	Reduced in size, bilateral	Intentionally Not Sampled
	THYROID	Increased in size	Hypertrophy/Hyperplasia, Follicular Cell
220	ADRENAL	Reduced in size, bilateral	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 3

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
220 (cont)	THYROID	Increased in size, bilateral	Hypertrophy/Hyperplasia, Follicular Cell
233	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
	LIVER	Mottled	Intentionally Not Sampled
	THYROID	Enlarged	Hypertrophy/Hyperplasia, Follicular Cell
238	LIVER	Reduced in size	Intentionally Not Sampled
	ADRENAL	Reduced in size, bilateral	Intentionally Not Sampled
	KIDNEY	Reduced in size, bilateral	Intentionally Not Sampled
	THYROID	Enlarged and reddened	Hypertrophy/Hyperplasia, Follicular Cell
251	LIVER	Ventral, reduced in size	Intentionally Not Sampled
	PROSTATE	Dorsolateral, reduced in size	Intentionally Not Sampled
	THYROID	Enlarged and reddened	Hypertrophy/Hyperplasia, Follicular Cell
256	LIVER	Reduced in size	Intentionally Not Sampled
	ADRENAL	Reduced in size, bilateral	Intentionally Not Sampled
	THYROID	Enlarged and reddened	Hypertrophy/Hyperplasia, Follicular Cell

08055.001
Terminal Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 4

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
139	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
	PROSTATE	Ventral, reduced in size	Intentionally Not Sampled
196	SEMINAL VESICLE	Right, reduced in size	Intentionally Not Sampled
214	PROSTATE	Ventral and dorsolateral, reduced in size	Intentionally Not Sampled
232	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
	PROSTATE	Dorsal, reduced in size	Intentionally Not Sampled

08055.001
Terminal Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 5

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
149	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled
158	SEMINAL VESICLE	Reduced in size, bilaterally	Intentionally Not Sampled
	PROSTATE	Ventral and dorsolateral, reduced in size	Intentionally Not Sampled
195	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
	PROSTATE	Ventral and dorsolateral, reduced in size	Intentionally Not Sampled
	PITUITARY	Reduced in size	Intentionally Not Sampled
204	SEMINAL VESICLE	Ventral/dorsolateral, with coagulating glands, reduced in size	Intentionally Not Sampled
231	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled
240	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled
249	PROSTATE	Ventral, reduced in size	Intentionally Not Sampled
258	SPLEEN	Enlarged white foci	Intentionally Not Sampled
	LUNG	Multiple reddened areas	Intentionally Not Sampled
	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled

08055.001
Terminal Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 6

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
177	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled
	PROSTATE	Dorsal, reduced in size	Intentionally Not Sampled
194	ADRENAL	Dark tan to brown in color	Intentionally Not Sampled
205	ADRENAL	Pale in color, both	Intentionally Not Sampled
212	ADRENAL	Slightly enlarged	Intentionally Not Sampled
223	KIDNEY	Right side, hydronephrosis	Intentionally Not Sampled
230	ADRENAL	Pale in color	Intentionally Not Sampled

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 7

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
160	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
178	ADRENAL	Enlarged	Intentionally Not Sampled
188	ADRENAL	Increased in size, bilateral	Intentionally Not Sampled
193	ADRENAL	Increased in size, bilateral	Intentionally Not Sampled
206	PROSTATE	Ventral and dorsolateral, reduced in size	Intentionally Not Sampled
	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
	ADRENAL	Enlarged, bilateral	Intentionally Not Sampled
211	PROSTATE	Ventral, reduced in size	Intentionally Not Sampled
	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled
	ADRENAL	Increased in size, bilateral	Intentionally Not Sampled
224	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled
229	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
	PROSTATE	Ventral, reduced in size	Intentionally Not Sampled
247	LUNG	Right, pinpoint foci	Intentionally Not Sampled
264	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
	ADRENAL	Left, increased in size	Intentionally Not Sampled

08055.001
Terminal Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 8

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
164	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
210	PROSTATE	Ventral and dorsolateral, reduced in size	Intentionally Not Sampled
	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
246	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled

08055.001
Terminal Sacrifice

CORRELATION OF GROSS AND MICROSCOPIC FINDINGS

Species: Rat Sex: Males Group Identification: 9

Animal Number	Client Topography / Site	Client Gross Observations	Microscopic Observations
163	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
181	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled
	PROSTATE	Dorsal, reduced in size	Intentionally Not Sampled
208	KIDNEY	Right, hydronephrosis	Intentionally Not Sampled
226	PROSTATE	Ventral and dorsolateral, reduced in size	Intentionally Not Sampled
	SEMINAL VESICLE	Reduced in size, bilateral	Intentionally Not Sampled
245	PROSTATE	Ventral, reduced in size	Intentionally Not Sampled
	SEMINAL VESICLE	Reduced in size	Intentionally Not Sampled

Appendix III

Analytical Chemistry Reports

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Atrazine in Mazola Corn Oil

November 10, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory
1529 West Sequim Bay Road
Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology
Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Atrazine in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Atrazine in Mazola Corn Oil

Parameter	Chemical
Compound Name	Atrazine
CAS #	1912-24-9
Central File No.	CF-1826
Initial Receipt Date	5/30/02
Expiration Date	01/2005
Manufacturer	ChemService, Inc
Lot Number	277-93B
Battelle Study #	WA 2-14-02-02
Method	SW 846, 8015B Modified

Executive Summary

The chemical purity of atrazine determined by the manufacturer was 98%. The purity result from Battelle-Sequim by GC-FID was determined to be 99.9%. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of atrazine was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 12 weeks. Thus, stability testing of the atrazine stock solution in Mazola corn oil was considered stable at both the 15 mg/mL and 30 mg/mL concentrations for the required testing and holding period of 12 weeks.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 105% to 114%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA 2-14-02-02, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of atrazine (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_Atrazine-cornoil.doc, PSTP_WA-2-14_Atrazine_cornoil.doc, DSUM_WA2-14_Atrazine-Fenarimol-crnoil.xls, and DAF_WA-2-14_Atrazine-Fenarimol-crnoil.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, atrazine, (CAS No. 1912-24-9) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Atrazine was purchased from ChemService, Inc and lot number 277-93B was initially received on 5/30/02 with an expiration date of 01/2005 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1826) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-02

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Atrazine (MSL CF 1826)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 15 mg/mL and 30 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Testing/holding duration: 12 weeks

Chemical Information

Chemical Name: Atrazine

CAS: 1912-24-9

Any known purity information: may refer to attached documentation

Manufacturer's Purity Information: 98% pure

Any known stability information: may refer to attached documentation

Manufacturer's Stability Information: stable

Desired purity (%) for test? 95% or greater

Figure 1. EDSP Requisition Form for Atrazine

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Atrazine
CAS #	1912-24-9
Central File No.	CF-1826
Initial Receipt Date	5/30/02
Expiration Date	01/2005
Manufacturer	ChemService, Inc
Lot Number	277-93B
Manufacturer's Purity	98%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA2-14-02-02
Method	SW 846, 8015B Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted by taking a solution in hexane of about 100 µg/mL. This matrix was then run on a gas chromatograph with a flame ionization detector (GC-FID). A blank hexane was also run on the GC-FID. The purity was determined by first identifying the peaks in the chromatogram of the atrazine that were the same as the peaks in the analysis of the hexane blank sample. The areas associated with these common peaks were then eliminated by inhibiting integration and the remaining peaks were reported as a percentage of the total peak area. The percentage associated with the largest peak represented the purity of atrazine. The GC was set up with an autosampler and a 30 mx 0.25 mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and the detector temperature at 320ºC. The autosampler was set to inject 1 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. Stock solutions were prepared at the chemical concentrations requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

Atrazine stock solutions were prepared on 8-22-02 for testing as described in Table 2. Briefly, for the 15 mg/mL atrazine solution, 3 g of atrazine was weighed into a 250 mL amber wide-mouth jar containing 180 g corn oil, a stir bar was added, and the solution was agitated on a stir plate to suspend the chemical. For the 30 mg/mL atrazine solution, 6 g was weighed into 180 g corn oil as described above. Again a stir bar was added, and the solution was mixed on a stir

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA 2-14-02-02 12 Weeks	Atrazine	15 mg/mL (15,000 µg/mL)	1826-1-2	3 g in 180 g Mazola corn oil
		30 mg/mL (30,000 µg/mL)	1826-1-3	6 g in 180 g Mazola corn oil

plate to suspend the chemical. All solutions were transferred to ashed, amber glass bottles. Bottles were labeled and stored at 4ºC ± 2ºC for the duration of the test.

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by chromatographic analysis. Triplicate aliquots of each concentration were tested. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

Atrazine stock solution was sampled by weighing ~1 g of sample into a 30 mL amber, ashed vial and adding 25 mL of methylene chloride using a volumetric pipette. For 1826-1-2, analysis was done by taking 0.1 mL of the hexane solution and 0.02 ml of internal standard REP7, 5a androstane and 0.88 mL of hexane. For 1826-1-3, 0.025 mL taken with 0.02 mL REP7 and 0.96 mL hexane. This solution was then analyzed on the GC-FID. A corn oil blank was prepared and analyzed in the same way. The major peak determined during the purity analysis of atrazine was used for this analysis. Continuing calibration verification (CCV) samples were analyzed to demonstrate on-going calibration accuracy.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a GC-FID purity scan on the atrazine. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for atrazine. The area of the atrazine peak was 99.9% of the total area of all peaks in the chromatogram. Chemical purity of atrazine determined by the manufacturer was 98% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 08/22/02. Chemical concentrations were determined over 12 sampling intervalsfrom 08/22/02 to 11/14/02. The analytical and quality control (QC) results are presented in Appendix C. A single preparation blank was analyzed with every sample batch. There were no detectable concentrations of atrazine in the blanks. CCV results ranged from 92.2% to 104%. Internal standards were analyzed with each sample and these results ranged from 91.3% to 113%. The MDL was 115 µg/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg, as required for biological testing (Appendix C). The average peroxide number in the Mazola corn oil with an expiration date of 6/03 was 1.77 meq/kg (RSD = 6.41%). The average peroxide number in the Mazola corn oil with an expiration date of 1/04 was 1.34 meq/kg (RSD = 8.31%).

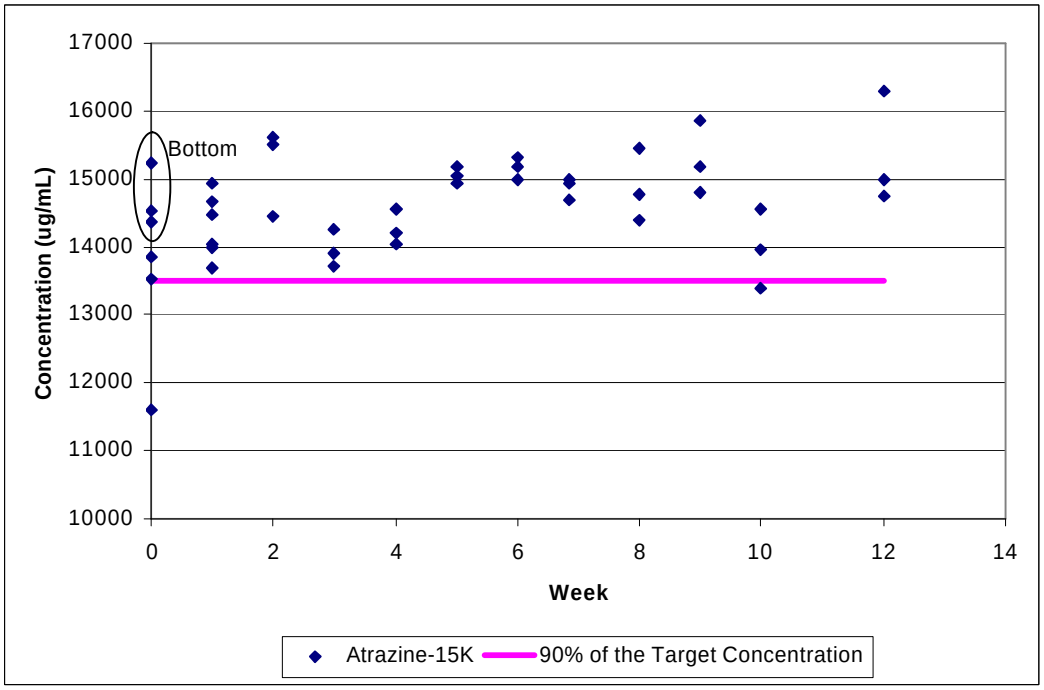
3.3 Statistical Results of Stability Trial

A plot of atrazine with a target concentration of 15,000 µg/mL against time shows very little decay in chemical concentration (Figure 2). All but two data points were greater than 90% of the target concentration. Homogeneity of the chemical concentration within the test container was evaluated at time 0 and at 1 week. At time 0, a significant difference was detected ($p = 0.05$) between the concentrations obtained from the top and bottom sections of the container, but the difference was no longer significant by week 1. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of atrazine was expected to stay greater than or equal to 90% of the target concentration for an unlimited amount of time (Table 3). Thus, this stock solution was considered stable for the required biological testing and holding period of 12 weeks. The complete statistical analysis is presented in Appendix D.

All observations of atrazine with a target concentration of 30,000 µg/mL were greater than 90% of the average target concentration (Figure 2). Homogeneity of the chemical concentration within the test container was evaluated at time 0 and at 1 week. At time 0, a significant difference was detected ($p = 0.05$) between the concentrations obtained from the top and bottom sections of the container, but the difference was no longer significant by week 1. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of atrazine was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 31 weeks (Table 3). Thus, this stock solution was considered stable for the required biological testing and holding period of 12 weeks. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses ranged from 105% to 114%. The complete analysis is presented in Appendix E.



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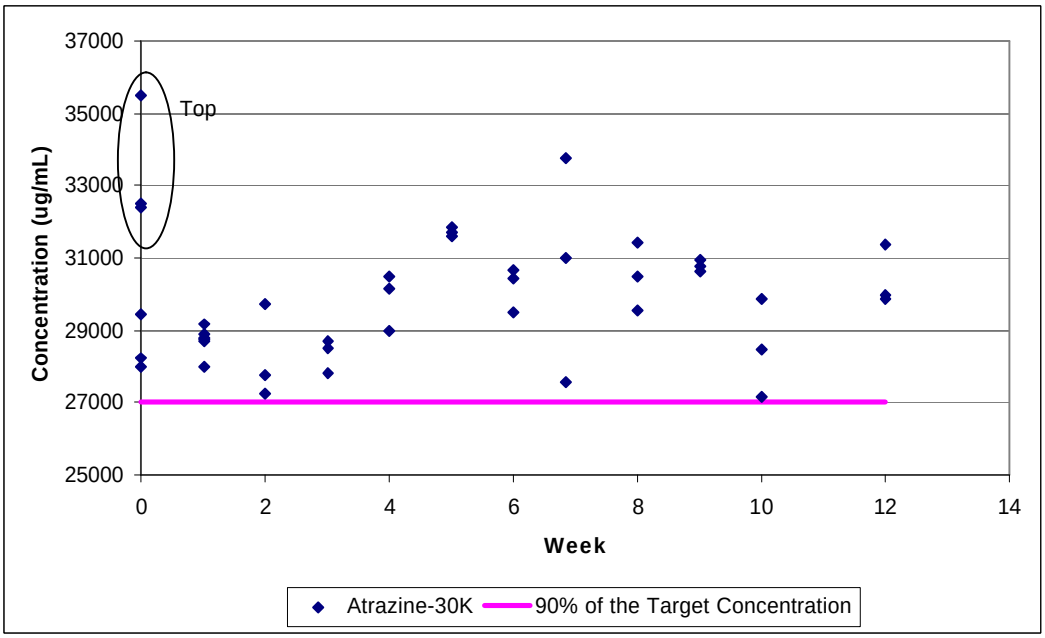


B

Figure 2. Observed Concentration of Atrazine with a Target Concentration of 15,000 mg/mL (A) and 30,000 mg/mL (B) Against Time

Table 3. Summary of Statistical Results for Atrazine

WA 2-14-02 Statistical Analysis conducted by Valerie Cullinan Using Minitab Version 13.32, Minitab Inc., 1999.	1826-1-2 Atrazine-15K	1826-1-3 Atrazine-30K
Target Concentration (μg/mL)	15000	30000
Number of determinations	1	1
Number of weeks tested	12	12
Number of replicates per day	3	3
Number of outliers removed	0	0
Number of observations removed	0	0
Overall Mean Concentration	14592	29913
95% Upper CL	14799	30376
error degrees of freedom	41	41
1-sample t-test of Ho: μ >= Target	S [a]	NS
estimated intercept of ln(concentration) against time	9.5586	10.2952
estimated slope of ln(concentration) against time	0.0058	0.0019
standard error of slope	0.0022	0.0024
error degrees of freedom	40	40
Significance test of lack-of-fit for final model	NS [b]	NS
Significance test of Ho: β = 0 vs. H1: β ? 0	S	NS
Lower 95% CL of β	0.001	-0.003
Upper 95% CL of β	0.010	0.007
Maximum Percent Loss (using LCL)	-1.1%	2.3%
Mean Percent Loss (using bhat)	-4.7%	-1.5%
LN(90% of Target)	9.5104	10.2036
Number of weeks until at 90% of Target (using LCL)	NA	31
Conclusion using Target Concentration:	**Stable for 12 wks**	**Stable for 12 wks**

[a] Significant at α = 0.05
[b] Not Significant at α = 0.05

4.0 CONCLUSIONS

Purity as determined by the manufacturer was 98%; Battelle-Sequim determined purity to be 99.9%. Stability testing of atrazine in Mazola corn oil concluded that the chemical was stable at both the 15 mg/mL and 30 mg/mL concentrations for a period of 12 weeks.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses ranged from 105% to 114%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

660 Tower Lane • P.O. Box 599 • West Chester, PA 19381-0599
1-800-452-9994 • 1-610-692-3026 • Fax 1-610-692-8729
info@chemservice.com • www.chemservice.com

CERTIFICATE OF ANALYSIS

INVOICE #: CS229018
PO #: 11114099EAC

CATALOG #: PS-380 CAS #: 1912-24-9

DESCRIPTION: Atrazine

LOT #: 277-93B

PURITY: 98%

EXPIRATION DATE: 01/05

Chem Service, Inc. guarantees the purity of this chemical ± 0.5% deviation prior to the expiration date shown on the label and exclusive of any customer contamination.

Two or more of the following methods of analysis are used to determine purity: Melting point, refractive index, titration, IR, TLC, GC/FID, GC/TCD, GC/ECD, GC/MS, HPLC or DSC.

Our standards are suitable for use with all EPA methods.

Certified By:

John Conrad

John Conrad
CSM/TC

ISO 9001

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Atrazine

Chemical Name: Atrazine (MSL CF 1826), CMS 173754

CAS Number: 1912-24-9

Lot Number: 277-93B, stored at RT in MSL5, Rm 219

Expiration date: 01/2005

Manufacturer's Purity Information: 98%

Manufacturer's Stability Information: stable

MSL Purity Results:
Purity (%) To be determined at MSL by GC-FID scan

MDL has not been determined.

Bioassay Information: Pesticide, see MSDS

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay:

Test Chemical: Atrazine

CAS: 1912-24-9

Carrier(s): Mazola corn oil

Concentrations/Dilution Series: 15 and 30 mg/mL

Below MDL determined in Purity Analysis?

In vitro or in vivo tests?: In vivo

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Testing/holding duration: 12 weeks

Design of Stability Test: Two concentrations, 15.0 mg/mL and 30.0 mg/mL in Mazola corn oil, will be tested. The chemical will be sieved through an 80 mesh screen and material that passes will be suspended in Mazola corn oil with a magnetic stirrer. Samples of the suspension will be taken with a gavage needle, while the suspension is being vigorously stirred, at mid-depth in a 250 mL amber glass bottle, except for the first sampling, which will be sampled at 25% and 75% depth in triplicate to demonstrate homogeneity. The suspension will be stored in glass at 4 deg. C in the dark for 12 weeks, sampled at least 8 times in triplicate and analyzed monthly by GC detector.

Number of replicates: 3

Duration: 12 weeks, sampling at least 8 time points with triplicate samples taken each time

Other factors:
Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other: None

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:
Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
    - Chemical repository confirmatory test results of chemical identity and purity;
    - Chemical repository test results of lot-to-lot variation in chemical purity;
    - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. Atrazine concentration in Mazola Corn Oil (µg/mL)

Target Concentration	Sample ID	Date	Atrazine	Average	RSD	Recovery[1]
15000 ug/ml	1826-1-2-1 top R-1	8/22/2002	13853			
15000 ug/ml	1826-1-2-1 top R-2	8/22/2002	11607	12999	9.35%	86.8%
15000 ug/ml	1826-1-2-1 top R-3	8/22/2002	13535			
15000 ug/ml	1826-1-2-1 bottom R-1	8/22/2002	15228			
15000 ug/ml	1826-1-2-1 bottom R-2	8/22/2002	14359	14708	3.12%	98.1%
15000 ug/ml	1826-1-2-1 bottom R-3	8/22/2002	14537			
30000 ug/ml	1826-1-3-1 top R-1	8/22/2002	32521			
30000 ug/ml	1826-1-3-1 top R-2	8/22/2002	35497	33474	5.24%	112%
30000 ug/ml	1826-1-3-1 top R-3	8/22/2002	32404			
30000 ug/ml	1826-1-3-1 bottom R-1	8/22/2002	29465			
30000 ug/ml	1826-1-3-1 bottom R-2	8/22/2002	27978	28554	2.80%	95.2%
30000 ug/ml	1826-1-3-1 bottom R-3	8/22/2002	28218			
Blank	Corn Oil (T=0)	8/22/2002	115 U			
15000 ug/ml	1826-1-2-2 top R-1	8/29/2002	14473			
15000 ug/ml	1826-1-2-2 top R-2	8/29/2002	14655	14376	2.35%	95.8%
15000 ug/ml	1826-1-2-2 top R-3	8/29/2002	14000			
15000 ug/ml	1826-1-2-2 bottom R-1	8/29/2002	13681			
15000 ug/ml	1826-1-2-2 bottom R-2	8/29/2002	14045	14218	4.50%	94.8%
15000 ug/ml	1826-1-2-2 bottom R-3	8/29/2002	14927			
30000 ug/ml	1826-1-3-2 top R-1	8/29/2002	28879			
30000 ug/ml	1826-1-3-2 top R-2	8/29/2002	29161	28907	0.84%	96.4%
30000 ug/ml	1826-1-3-2 top R-3	8/29/2002	28680			
30000 ug/ml	1826-1-3-2 bottom R-1	8/29/2002	28757			
30000 ug/ml	1826-1-3-2 bottom R-2	8/29/2002	27993	28516	1.59%	95.1%
30000 ug/ml	1826-1-3-2 bottom R-3	8/29/2002	28799			
Blank	Corn oil (week 1)	8/29/2002	115 U			
Blank	Corn oil (week 1)	8/29/2002	115 U			
15000 ug/ml	1826-1-2-3 R-1	9/5/2002	14450			
15000 ug/ml	1826-1-2-3 R-2	9/5/2002	15502	15187	4.21%	101%
15000 ug/ml	1826-1-2-3 R-3	9/5/2002	15607			
30000 ug/ml	1826-1-3-3 R-1	9/5/2002	29748			
30000 ug/ml	1826-1-3-3 R-2	9/5/2002	27271	28258	4.65%	94.2%
30000 ug/ml	1826-1-3-3 R-3	9/5/2002	27753			
Blank	Corn oil (week 2)	9/5/2002	115 U			
15000 ug/ml	1826-1-2-4 R-1	9/12/2002	13902			
15000 ug/ml	1826-1-2-4 R-2	9/12/2002	14254	13956	1.97%	93.0%
15000 ug/ml	1826-1-2-4 R-3	9/12/2002	13713			
30000 ug/ml	1826-1-3-4 R-1	9/12/2002	27792			
30000 ug/ml	1826-1-3-4 R-2	9/12/2002	28508	28336	1.70%	94.5%
30000 ug/ml	1826-1-3-4 R-3	9/12/2002	28709			
Blank	Corn oil (week 3)	9/12/2002	115 U			
15000 ug/ml	1826-1-2-5 R-1	9/19/2002	14050			
15000 ug/ml	1826-1-2-5 R-2	9/19/2002	14571	14272	1.88%	95.1%
15000 ug/ml	1826-1-2-5 R-3	9/19/2002	14194			

Table C1. Continued

Target Concentration	Sample ID	Date	Atrazine	Average	RSD	Recovery[1]
30000 ug/ml	1826-1-3-5 R-1	9/19/2002	29006			
30000 ug/ml	1826-1-3-5 R-2	9/19/2002	30502	29886	2.62%	99.6%
30000 ug/ml	1826-1-3-5 R-3	9/19/2002	30149			
Blank	Corn oil (week 4)	9/19/2002	115 U			
15000 ug/ml	1826-1-2-6 R-1	9/26/2002	15194			
15000 ug/ml	1826-1-2-6 R-2	9/26/2002	14938	15063	0.85%	100%
15000 ug/ml	1826-1-2-6 R-3	9/26/2002	15057			
30000 ug/ml	1826-1-3-6 R-1	9/26/2002	31851			
30000 ug/ml	1826-1-3-6 R-2	9/26/2002	31609	31718	0.39%	106%
30000 ug/ml	1826-1-3-6 R-3	9/26/2002	31693			
Blank	Corn oil (week 5)	9/26/2002	115 U			
15000 ug/ml	1826-1-2-7 R-1	10/3/2002	14998			
15000 ug/ml	1826-1-2-7 R-2	10/3/2002	15178	15161	1.02%	101%
15000 ug/ml	1826-1-2-7 R-3	10/3/2002	15307			
30000 ug/ml	1826-1-3-7 R-1	10/3/2002	30661			
30000 ug/ml	1826-1-3-7 R-2	10/3/2002	30438	30201	2.03%	101%
30000 ug/ml	1826-1-3-7 R-3	10/3/2002	29504			
Blank	Corn oil (week 6)	10/3/2002	115 U			
15000 ug/ml	1826-1-2-8 R-1	10/10/2002	14696			
15000 ug/ml	1826-1-2-8 R-2	10/10/2002	14929	14875	1.07%	99.2%
15000 ug/ml	1826-1-2-8 R-3	10/10/2002	15000			
30000 ug/ml	1826-1-3-8 R-1	10/10/2002	33760			
30000 ug/ml	1826-1-3-8 R-2	10/10/2002	31014	30788	10.04%	103%
30000 ug/ml	1826-1-3-8 R-3	10/10/2002	27589			
Blank	Corn oil (week 7)	10/102002	115 U			
15000 ug/ml	1826-1-2-9 R-1	10/17/2002	14389			
15000 ug/ml	1826-1-2-9 R-2	10/17/2002	14775	14873	3.63%	99.2%
15000 ug/ml	1826-1-2-9 R-3	10/17/2002	15456			
30000 ug/ml	1826-1-3-9 R-1	10/17/2002	29528			
30000 ug/ml	1826-1-3-9 R-2	10/17/2002	31405	30480	3.08%	102%
30000 ug/ml	1826-1-3-9 R-3	10/17/2002	30506			
Blank	Corn oil (week 8)	10/17/2002	115 U			
15000 ug/ml	1826-1-2-10 R-1	10/24/2002	15176			
15000 ug/ml	1826-1-2-10 R-2	10/24/2002	15868	15278	3.58%	102%
15000 ug/ml	1826-1-2-10 R-3	10/24/2002	14790			
30000 ug/ml	1826-1-3-10 R-1	10/24/2002	30611			
30000 ug/ml	1826-1-3-10 R-2	10/24/2002	30947	30778	0.55%	103%
30000 ug/ml	1826-1-3-10 R-3	10/24/2002	30776			
Blank	Corn oil (week 9)	10/24/2002	115 U			
15000 ug/ml	1826-1-2-11 R-1	10/31/2002	13973			
15000 ug/ml	1826-1-2-11 R-2	10/31/2002	14565	13972	4.24%	93.2%
15000 ug/ml	1826-1-2-11 R-3	10/31/2002	13379			
30000 ug/ml	1826-1-3-11 R-1	10/31/2002	28468			
30000 ug/ml	1826-1-3-11 R-2	10/31/2002	29871	28492	4.80%	95.0%
30000 ug/ml	1826-1-3-11 R-3	10/31/2002	27137			
Blank	Corn oil (week 10)	10/31/2002	115 U			

Table C1. Continued

Target Concentration	Sample ID	Date	Atrazine	Average	RSD	Recovery[1]
15000 ug/ml	1826-1-2-12 R-1	11/14/2002	14760			
15000 ug/ml	1826-1-2-12 R-2	11/14/2002	14984	15346	5.40%	102%
15000 ug/ml	1826-1-2-12 R-3	11/14/2002	16294			
30000 ug/ml	1826-1-3-12 R-1	11/14/2002	29858			
30000 ug/ml	1826-1-3-12 R-2	11/14/2002	29952	30392	2.78%	99.7%
30000 ug/ml	1826-1-3-12 R-3	11/14/2002	31366			
Blank	Corn oil (week 12)	11/14/2002	115 U			

[1] Recovery is relative to the target concentration

U = Not detected at a value greater than the MDL

Table C.2. CCV Data for Atrazine Concentration in Mazola Corn Oil

Time	Sample Name	Atrazine (µg/mL)	Recovery	PD
T=0	EDSP Mix1 5 ug/ml	4.85	97.0%	3.00%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
Week 1	EDSP Mix1 5 ug/ml	4.77	95.4%	4.60%
	EDSP Mix1 5 ug/ml	4.95	99.0%	1.00%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	5.07	101%	1.40%
	EDSP Mix1 5 ug/ml	5.11	102%	2.20%
	EDSP Mix1 5 ug/ml	5.10	102%	2.00%
Week 2	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.11	102%	2.20%
	EDSP Mix1 5 ug/ml	5.10	102%	2.00%
Week 3	EDSP Mix1 5 ug/ml	4.80	96.0%	4.00%
	EDSP Mix1 5 ug/ml	4.92	98.4%	1.60%
	EDSP Mix1 5 ug/ml	4.88	97.6%	2.40%
Week 4	EDSP Mix1 5 ug/ml	4.84	96.8%	3.20%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.60%
	EDSP Mix1 5 ug/ml	4.92	98.4%	1.60%
Week 5	EDSP Mix1 5 ug/ml	4.96	99.2%	0.80%
	EDSP Mix1 5 ug/ml	5.16	103%	3.20%
	EDSP Mix1 5 ug/ml	5.11	102%	2.20%
Week 6	EDSP Mix1 5 ug/ml	4.61	92.2%	7.80%
	EDSP Mix1 5 ug/ml	5.18	104%	3.60%
	EDSP Mix1 5 ug/ml	5.18	104%	3.60%
Week 7	EDSP Mix1 5 ug/ml	4.92	98.4%	1.60%
	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
Week 8	EDSP Mix1 5 ug/ml	4.79	95.8%	4.20%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.60%
Week 9	EDSP Mix1 5 ug/ml	4.82	96.4%	3.60%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
Week 10	EDSP Mix1 5 ug/ml	4.76	95.2%	4.80%
	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.60%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
Week 12	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.05	101%	1.00%

Text Box C1. Calibration Standard Preparation

Calibration Standard EDSP Mix 1
Calibrations were performed using a five-point calibration curve labeled EDSP Mix 1 A thru E. This mix is used for Atrazine, Fenarimol, p,p'-DDE, Methoxychlor and Vinclozolin analyzed by GC-FID. These standards were made by serial dilutions of standards for each compound. • Atrazine standard was made by weighing 0.0499 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with Methylene chloride and labeled 1826-1-1. • Fenarimol standard was made by weighing 0.0506 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1829B-1. • p,p'-DDE standard was made by weighing 0.0501 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1832-1a-1. • Methoxychlor standard was made by weighing 0.0513 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1808-1-3. • Vinclozolin standard was made by weighing 0.0512 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1779-78. This analysis used an internal standard, in this case 5a androstane, which is made by weighing 0.0511 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane, this is then labeled REP7. The EDSP Mix 1 series (A through E) was made as follows. • Solution A, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 0.02 ml REP7 added to a 10 ml volumetric flask and diluted to the mark with hexane. • Solution B, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution C, 0.25 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution D, 0.1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane. • Solution E, 0.05 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane.

Table C.3. Internal Standards Data for Atrazine in Mazola Corn Oil

Sample Name	Date	5A androstane Recovery
Corn oil	8/22/2002	101%
1826-1-2-1 top R-1	8/22/2002	104%
1826-1-2-1 top R-2	8/22/2002	108%
1826-1-2-1 top R-3	8/22/2002	109%
1826-1-2-1 bottom R-1	8/22/2002	107%
1826-1-2-1 bottom R-2	8/22/2002	108%
1826-1-2-1 bottom R-3	8/22/2002	110%
1826-1-3-1 top R-1	8/22/2002	107%
1826-1-3-1 top R-2	8/22/2002	110%
1826-1-3-1 top R-3	8/22/2002	108%
1826-1-3-1 bottom R-1	8/22/2002	107%
1826-1-3-1 bottom R-2	8/22/2002	106%
1826-1-3-1 bottom R-3	8/22/2002	107%
Corn oil	8/29/2002	101%
1826-1-2-2 top R-1	8/29/2002	109%
1826-1-2-2 top R-2	8/29/2002	111%
1826-1-2-2 top R-3	8/29/2002	113%
1826-1-2-2 bottom R-1	8/29/2002	112%
1826-1-2-2 bottom R-2	8/29/2002	111%
1826-1-2-2 bottom R-3	8/29/2002	111%
1826-1-3-2 top R-1	8/29/2002	109%
1826-1-3-2 top R-2	8/29/2002	111%
1826-1-3-2 top R-3	8/29/2002	110%
1826-1-3-2 bottom R-1	8/29/2002	108%
1826-1-3-2 bottom R-2	8/29/2002	110%
1826-1-3-2 bottom R-3	8/29/2002	109%
Corn oil	9/5/2002	100%
1826-1-2-3 R-1	9/5/2002	109%
1826-1-2-3 R-2	9/5/2002	103%
1826-1-2-3 R-3	9/5/2002	108%
1826-1-3-3 R-1	9/5/2002	105%
1826-1-3-3 R-2	9/5/2002	107%
1826-1-3-3 R-3	9/5/2002	107%
Corn oil	9/12/2002	112%
1826-1-2-4 R-1	9/12/2002	102%
1826-1-2-4 R-2	9/12/2002	105%
1826-1-2-4 R-3	9/12/2002	106%
1826-1-3-4 R-1	9/12/2002	103%
1826-1-3-4 R-2	9/12/2002	104%
1826-1-3-4 R-3	9/12/2002	103%

Table C.3, Continued

Sample Name	Date	5A androstane Recovery
Corn oil	9/19/2002	97.1%
1826-1-2-5 R-1	9/19/2002	100%
1826-1-2-5 R-2	9/19/2002	98.9%
1826-1-2-5 R-3	9/19/2002	101%
1826-1-3-5 R-1	9/19/2002	96.5%
1826-1-3-5 R-2	9/19/2002	97.4%
1826-1-3-5 R-3	9/19/2002	99.2%
Corn oil	9/26/2002	101%
1826-1-2-6 R-1	9/26/2002	106%
1826-1-2-6 R-2	9/26/2002	106%
1826-1-2-6 R-3	9/26/2002	106%
1826-1-3-6 R-1	9/26/2002	104%
1826-1-3-6 R-2	9/26/2002	104%
1826-1-3-6 R-3	9/26/2002	102%
Corn oil	10/3/2002	99.2%
1826-1-2-7 R-1	10/3/2002	107%
1826-1-2-7 R-2	10/3/2002	106%
1826-1-2-7 R-3	10/3/2002	103%
1826-1-3-7 R-1	10/3/2002	101%
1826-1-3-7 R-2	10/3/2002	105%
1826-1-3-7 R-3	10/3/2002	105%
Corn oil	10/10/2002	96.6%
1826-1-2-8 R-1	10/10/2002	101%
1826-1-2-8 R-2	10/10/2002	98.8%
1826-1-2-8 R-3	10/10/2002	99.0%
1826-1-3-8 R-1	10/10/2002	98.2%
1826-1-3-8 R-2	10/10/2002	96.6%
1826-1-3-8 R-3	10/10/2002	96.8%
Corn oil	10/17/2002	96.7%
1826-1-2-9 R-1	10/17/2002	104%
1826-1-2-9 R-2	10/17/2002	101%
1826-1-2-9 R-3	10/17/2002	97.1%
1826-1-3-9 R-1	10/17/2002	100%
1826-1-3-9 R-2	10/17/2002	97.1%
1826-1-3-9 R-3	10/17/2002	98.5%
Corn oil	10/24/2002	98.0%
1826-1-2-10 R-1	10/24/2002	101%
1826-1-2-10 R-2	10/24/2002	99.5%
1826-1-2-10 R-3	10/24/2002	101%
1826-1-3-10 R-1	10/24/2002	98.3%
1826-1-3-10 R-2	10/24/2002	100%
1826-1-3-10 R-3	10/24/2002	98.6%

Table C.3, Continued

Sample Name	Date	5A androstane Recovery
Corn oil	10/31/2002	97.2%
1826-1-2-11 R-1	10/31/2002	106%
1826-1-2-11 R-2	10/31/2002	104%
1826-1-2-11 R-3	10/31/2002	111%
1826-1-3-11 R-1	10/31/2002	104%
1826-1-3-11 R-2	10/31/2002	101%
1826-1-3-11 R-3	10/31/2002	109%
Corn oil	11/14/2002	101%
1826-1-2-12 R-1	11/14/2002	99.5%
1826-1-2-12 R-2	11/14/2002	99.3%
1826-1-2-12 R-3	11/14/2002	91.3%
1826-1-3-12 R-1	11/14/2002	97.9%
1826-1-3-12 R-2	11/14/2002	96.7%
1826-1-3-12 R-3	11/14/2002	97.3%

Table C.4. Peroxide Concentration in Mazola Corn Oil (meq/kg)

Sample	Analysis Date	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	09/05/02	0.5	0.005	5.00	0.50		
Mazola Corn Oil Expiration 6-03 R-1	09/05/02	1.9	0.005	5.01	1.90		
Mazola Corn Oil Expiration 6-03 R-2	09/05/02	1.8	0.005	5.36	1.68	1.77	6.41
Mazola Corn Oil Expiration 6-03 R-3	09/05/02	1.8	0.005	5.16	1.74		
Mazola Corn Oil Expiration 1-04 R-1	09/05/02	1.2	0.005	4.92	1.22		
Mazola Corn Oil Expiration 1-04 R-2	09/05/02	1.5	0.005	5.2	1.44	1.34	8.31
Mazola Corn Oil Expiration 1-04 R-3	09/05/02	1.4	0.005	5.13	1.36		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-02
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.
1/24/2003 2:48:30 PM

Subset worksheet Week 0 created.
Subset worksheet Week 1 created.

Results for: Week 0

Two-Sample T-Test and CI: Atrazine-15K, section

Two-sample T for Atrazine-15K

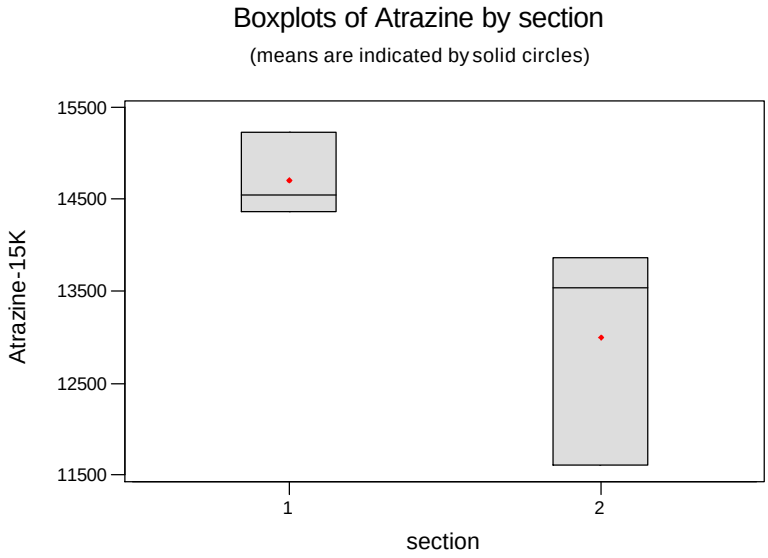
1 = bottom
2 = top

section	N	Mean	StDev	SE Mean
1	3	14708	459	265
2	3	12999	1215	702

Very poor power!

Difference = mu (1) - mu (2)
Estimate for difference: 1709
95% CI for difference: (-1518, 4936)
T-Test of difference = 0 (vs not =): T-Value = 2.28 P-Value = 0.150 DF = 2

NS



Kruskal-Wallis Test: Atrazine-15K versus section

Kruskal-Wallis Test on Atrazine

section	N	Median	Ave Rank	Z
1	3	14537	5.0	1.96
2	3	13535	2.0	-1.96
Overall	6		3.5	

H = 3.86 DF = 1 P = 0.050

Sections are significantly different.

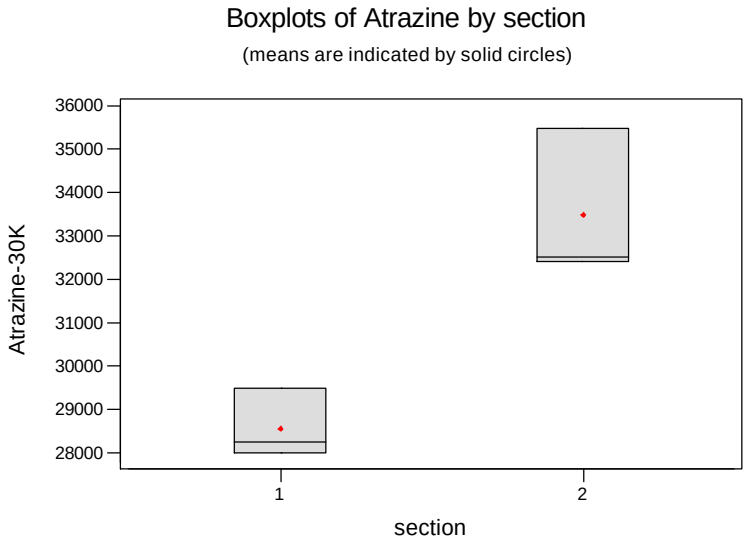
* NOTE * One or more small samples

Two-Sample T-Test and CI: Atrazine-30K, section

Two-sample T for Atrazine-30K

section	N	Mean	StDev	SE Mean
1	3	28554	798	461
2	3	33474	1753	1012

Difference = mu (1) - mu (2)
Estimate for difference: -4920
95% CI for difference: (-9706, -134)
T-Test of difference = 0 (vs not =): T-Value = -4.42 P-Value = 0.047 DF = 2



Sections are significantly different.

Kruskal-Wallis Test: Atrazine-30K versus section

Kruskal-Wallis Test on Atrazine

section	N	Median	Ave Rank	Z
1	3	28218	2.0	-1.96
2	3	32521	5.0	1.96
Overall	6		3.5	

H = 3.86 DF = 1 P = 0.050

* NOTE * One or more small samples

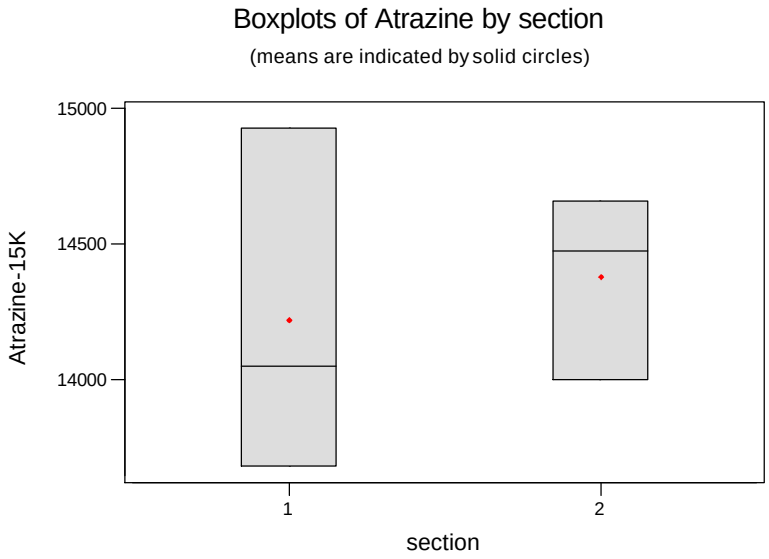
Results for: Week 1

Two-Sample T-Test and CI: Atrazine-15K, section

Two-sample T for Atrazine-15K

section	N	Mean	StDev	SE Mean
1	3	14218	640	370
2	3	14376	338	195

Difference = mu (1) - mu (2)
Estimate for difference: -159
95% CI for difference: (-1489, 1172)
T-Test of difference = 0 (vs not =): T-Value = -0.38 P-Value = 0.730 DF = 3



Can't reject the null that sections are the same.

Kruskal-Wallis Test: Atrazine-15K versus section

Kruskal-Wallis Test on Atrazine

section	N	Median	Ave Rank	Z
1	3	14045	3.3	-0.22
2	3	14473	3.7	0.22
Overall	6		3.5	

H = 0.05 DF = 1 P = 0.827

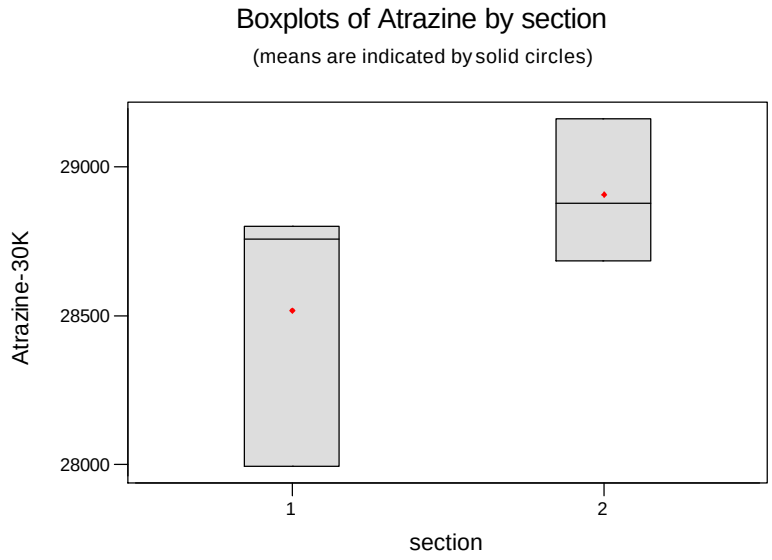
* NOTE * One or more small samples

Two-Sample T-Test and CI: Atrazine-30K, section

Two-sample T for Atrazine-30K

section	N	Mean	StDev	SE Mean
1	3	28516	454	262
2	3	28907	241	139

Difference = mu (1) - mu (2)
Estimate for difference: -391
95% CI for difference: (-1335, 554)
T-Test of difference = 0 (vs not =): T-Value = -1.32 P-Value = 0.279 DF = 3



Can't reject the null that sections are the same.

Kruskal-Wallis Test: Atrazine-30K versus section

Kruskal-Wallis Test on Atrazine

section	N	Median	Ave Rank	Z
1	3	28757	2.7	-1.09
2	3	28879	4.3	1.09
Overall	6		3.5	

H = 1.19 DF = 1 P = 0.275

* NOTE * One or more small samples

Conclusion: All test between sections have very poor power. For the week 0 data, both concentrations show a significant difference between the two sections.

By week 1, neither of the sections can be detected as significantly different.

Stability Data

3/4/2003 12:29:24 PM

- Performs a one-sample t-test for mu less than TARGET &

What is the target value for X 4
DATA> 15000

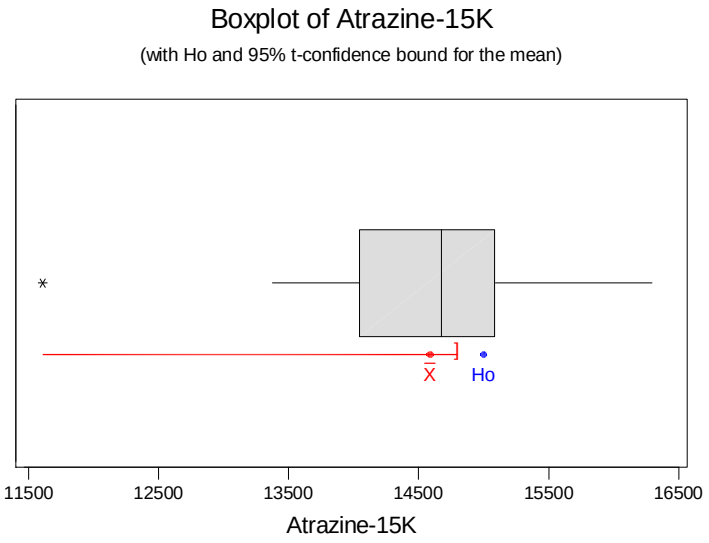
One-Sample T: Atrazine-15K

Test of mu = 15000 vs mu < 15000

Variable	N	Mean	StDev	SE Mean
Atrazine-15K	42	14592	798	123

Variable	95.0% Upper Bound	T	P
Atrazine-15K	14799	-3.32	0.001

t Boxplot of Atrazine-15K



- Outliers are < Median-3*IQD OR > Median+3*IQD

Boundary for outliers are values < 11561.9 and > 17789.6

No outliers

- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	9.6309
0	1	9.5721
0	1	9.5844
0	2	9.5363
0	2	9.3594
0	2	9.5131
1	1	9.5238
1	1	9.5500
1	1	9.6109
1	2	9.5801
1	2	9.5925
1	2	9.5468
2	0	9.5785
2	0	9.6487
2	0	9.6555
3	0	9.5398
3	0	9.5648
3	0	9.5261
4	0	9.5504
4	0	9.5868
4	0	9.5606
5	0	9.6287
5	0	9.6116
5	0	9.6196
6	0	9.6157
6	0	9.6276
6	0	9.6361
7	0	9.5954
7	0	9.6111
7	0	9.6158
8	0	9.5742
8	0	9.6007
8	0	9.6457
9	0	9.6274
9	0	9.6721
9	0	9.6017
10	0	9.5449
10	0	9.5864
10	0	9.5015
12	0	9.5997
12	0	9.6147
12	0	9.6986

- Conducts Simple Linear Regression

Regression Analysis: Atrazine-15K versus week

The regression equation is
Atrazine-15K = 9.56 + 0.00578 week

Predictor	Coef	SE Coef	T	P
Constant	9.55862	0.01329	719.29	0.000
week	0.005776	0.002160	2.67	0.011

S = 0.05287 R-Sq = 15.2% R-Sq(adj) = 13.0%

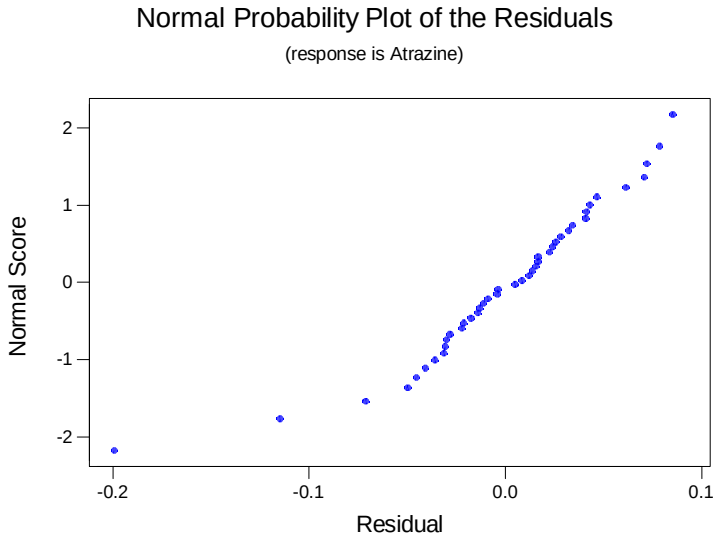
Analysis of Variance

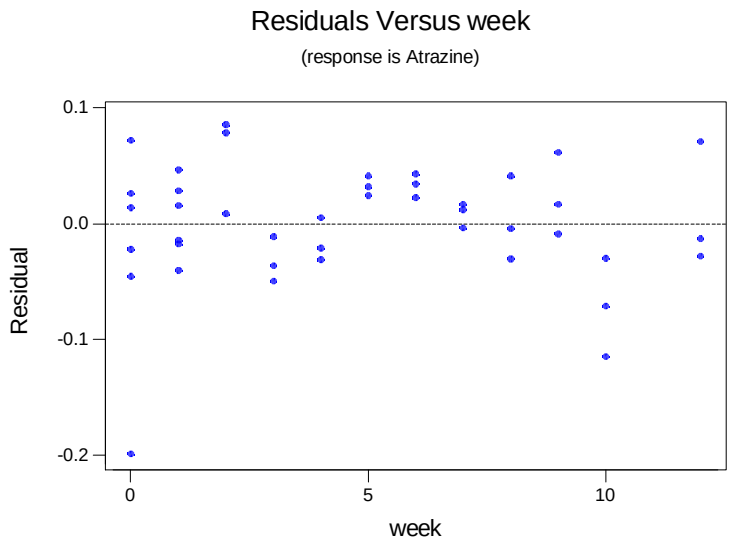
Source	DF	SS	MS	F	P
Regression	1	0.019987	0.019987	7.15	0.011
Residual Error	40	0.111796	0.002795		
Lack of Fit	10	0.042060	0.004206	1.81	0.102
Pure Error	30	0.069736	0.002325		
Total	41	0.131783			

Unusual Observations

Obs	week	Atrazine	Fit	SE Fit	Residual	St Resid
5	0.0	9.35940	9.55862	0.01329	-0.19922	-3.89R
39	10.0	9.50146	9.61638	0.01378	-0.11492	-2.25R

R denotes an observation with a large standardized residual





Do you want to remove any data points? (yes OR no)
no

Should a quadratic be fit? (yes OR no)
no

- Power analysis for t-test of slope less than zero

Power and Sample Size

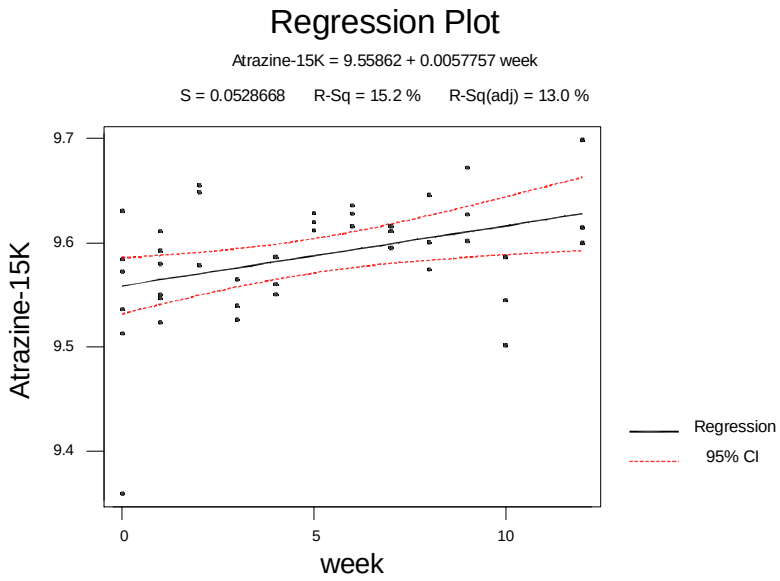
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05 Sigma = 0.0528668

Sample
Size Power Difference
40 0.9900 -0.0338

- That means we would detect a mean of 9.582 as significantly less than ln(15000) = 9.6158 or a change of 14501 from 15000 = 3.3% loss.

Fitted Line Plot: Atrazine-15K versus week



- **Conclusion – stable for 12 weeks.**

- Performs a one-sample t-test for mu less than TARGET &

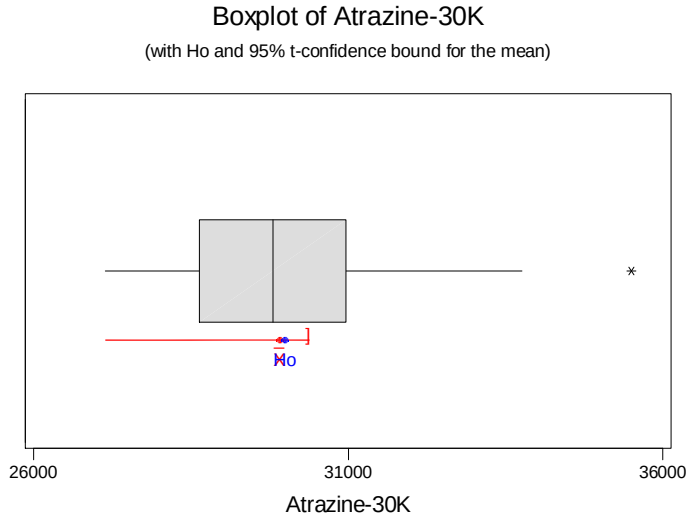
What is the target value for X 5
DATA> 30000

One-Sample T: Atrazine-30K

Test of mu = 30000 vs mu < 30000

Variable	N	Mean	StDev	SE Mean
Atrazine-30K	42	29913	1783	275

Variable	95.0% Upper Bound	T	P
Atrazine-30K	30376	-0.32	0.376



- Outliers are < Median-3*IQD OR > Median+3*IQD

Boundary for outliers are values < 22822.9 and > 36783.3
No outliers

- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	10.2910
0	1	10.2392
0	1	10.2477
0	2	10.3896
0	2	10.4772
0	2	10.3860
1	1	10.2666
1	1	10.2397
1	1	10.2681
1	2	10.2709
1	2	10.2806
1	2	10.2640
2	0	10.3005
2	0	10.2136
2	0	10.2311
3	0	10.2325
3	0	10.2579
3	0	10.2650
4	0	10.2753
4	0	10.3255
4	0	10.3139
5	0	10.3688
5	0	10.3612
5	0	10.3638
6	0	10.3308
6	0	10.3234
6	0	10.2923
7	0	10.4270
7	0	10.3422
7	0	10.2252
8	0	10.2931
8	0	10.3547
8	0	10.3257
9	0	10.3291
9	0	10.3400
9	0	10.3345
10	0	10.2565
10	0	10.3046
10	0	10.2087
12	0	10.3042
12	0	10.3074
12	0	10.3535

- Conducts Simple Linear Regression

The regression equation is
Atrazine-30K = 10.3 + 0.00188 week

Predictor	Coef	SE Coef	T	P
Constant	10.2952	0.0148	697.01	0.000
week	0.001881	0.002401	0.78	0.438

S = 0.05876 R-Sq = 1.5% R-Sq(adj) = 0.0%

Analysis of Variance

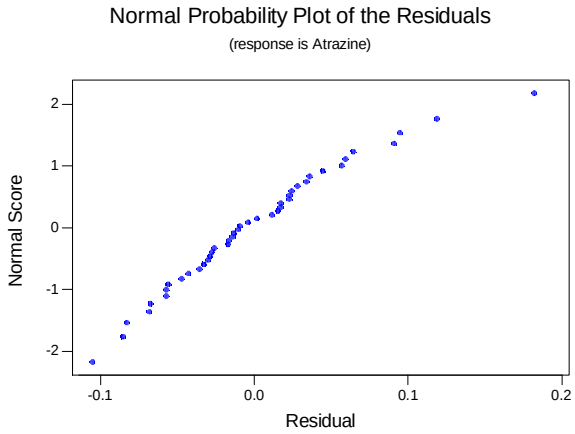
Source	DF	SS	MS	F	P
Regression	1	0.002119	0.002119	0.61	0.438
Residual Error	40	0.138112	0.003453		
Lack of Fit	10	0.057009	0.005701	2.11	0.056
Pure Error	30	0.081103	0.002703		
Total	41	0.140231			

Unusual Observations

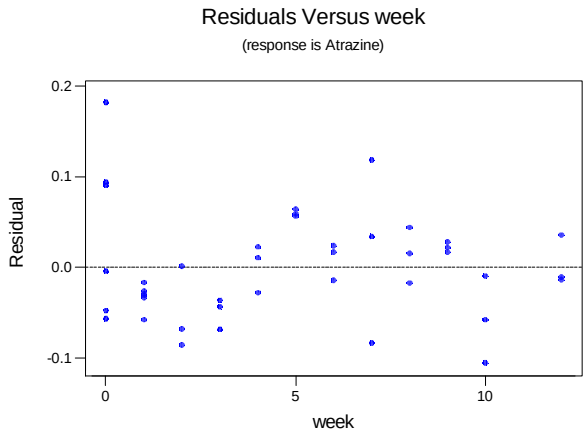
Obs	week	Atrazine	Fit	SE Fit	Residual	St Resid
5	0.0	10.4772	10.2952	0.0148	0.1820	3.20R
28	7.0	10.4270	10.3084	0.0104	0.1187	2.05R

R denotes an observation with a large standardized residual

Normplot of Residuals for Atrazine



Residuals from Atrazine vs week



Do you want to remove any data points? (yes OR no)
no
Should a quadratic be fit? (yes OR no)
no

- Power analysis for t-test of slope less than zero

Power and Sample Size

1-Sample t Test

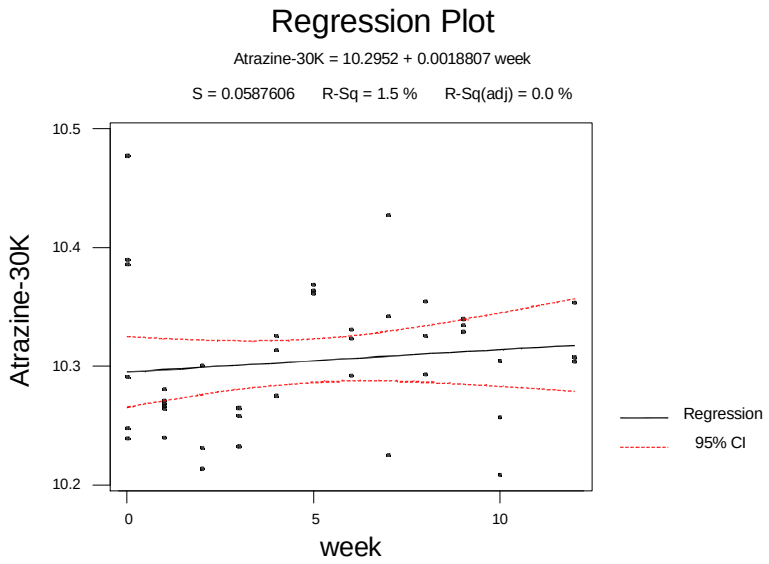
Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05 Sigma = 0.05876

Sample
Size Power Difference
40 0.9900 -0.0376

- That means we would detect a mean of 10.271 as significantly less than ln(30000) = 10.309 or a change of 28893 from 30000 = 3.7% loss.

- Fit 95% confidence bands about the fitted simple linear model

Fitted Line Plot: Atrazine-30K versus week



- **Conclusion – stable for 12 weeks.**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Atrazine in-life test suspension samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Atrazine suspended in corn oil

TEST SOLUTION SAMPLE CUSTODY AND PROCESSING: Test suspension samples were prepared by the EDSP Chemical Repository, Sequim, WA, using atrazine (CAS 1912-24-9, CF 1848, Chem Service lot # 285-63B, expiration date 6/05, 98% purity; CF 1898, Chem Service lot # 289-102A, expiration date 9/05, 98% purity; and CF 1826, Chem Service lot # 277-93B, expiration date 11/05, 98% purity) suspended in Mazola corn oil (corn oil was from containers with the following expiration dates: 6/12/03, 1/1/04, and 4/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time. Samples were prepared at two test concentrations for all replicates and exposures: 15 mg/mL and 30 mg/mL. The 15 mg/mL concentration was prepared by suspending 3.0 g of atrazine in 183 g of corn oil in a pre-cleaned, amber-glass container. The 30 mg/mL concentration was prepared by suspending 6.0 g of atrazine in 180 g of corn oil. Atrazine was sieved through an 80-mesh screen prior to use.

Samples for female rat exposures were prepared at two different times:
Replicate 1 – prepared on 09/09/02 and shipped on 09/10/02
Replicate 2 – prepared on 09/15/02 and shipped on 09/16/02.
Results of verification of concentrations for Replicate 1 are presented in Table 1.

Samples for male rat exposures were prepared at three different times:
Replicate 1 – prepared on 09/25/02 and shipped on 09/26/02
Replicate 2 – prepared on 10/02/02 and shipped on 10/03/02
Replicate 3 – prepared on 11/03/02 and shipped on 11/04/02.
Results of verification of concentrations for Replicates 1 and 2 are presented in Table 2.

The test suspension was sampled four times during the female test (9/18/02, 9/24/02, 10/01/02, and 10/08/02). Data are reported in Table 3. The test suspension was sampled four times during the male test (10/7/02, 10/14/02, 10/21/02, and 10/28/02). Data are reported in Table 4. Remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test were also returned and are reported in Table 5.

Processing

Test Suspension Samples for Concentration Verification Prior to Shipping:

The container was placed on a magnetic stir plate and stirred. Triplicate 1 mL samples from the top (about 0.25 inches below the surface) and bottom (about 1 inch from the bottom) of the container were sampled and placed in a tared, 30 mL, amber-glass bottle. The weight of the sample was determined

gravimetrically. A 1 g subsample was removed, placed in a 30 mL, amber ashed vial, and 25 mL of methylene chloride (MeCl) was added and the bottle agitated to mix. Then, 0.1 mL sample and 0.02 mL internal standard, 5a androstane, and 0.88 mL hexane were transferred to an auto sampler vial.

In-life and Returned Container Samples:

For the containers with sufficient material to analyze, the containers with remaining dosing solution were removed from the refrigerator, allowed to warm to room temperature, and then stirred using a magnetic stir bar and stir plate. About 1 mL was sampled and placed in a tared, 30 mL, amber-glass bottle. The weight of the sample was determined gravimetrically. 25 mL of MeCl was added and the bottle agitated to mix. For the 15 mg/mL solutions, 0.1 mL was transferred to a 1.8-mL vial with 0.02 mL of internal standard solution containing 5a androstane and 0.88 mL hexane. For the 30 mg/mL solutions, 0.025 mL was transferred to a 1.8-mL vial with 0.02 mL of internal standard solution containing 5a androstane and 0.955 mL hexane.

The in-life samples were returned in 20 mL scintillation vials, which contained a suspension with the atrazine settled to the bottom. The entire sample was extracted to ensure accurate analysis. The vial was weighed and the contents poured into a 60-mL, amber-glass bottle. 50 mL of MeCl was used for these samples. The scintillation vial was rinsed with part of the 50 mL MeCl; this rinse was then poured into the amber vial and the rinsing repeated to ensure complete transfer of the sample. The empty vial was dried and re-weighed. The amber bottles were agitated to mix, and 0.01 mL transferred to an auto sampler vial with 0.02 mL of internal standard solution containing 5a androstane and 0.97 mL hexane.

SAMPLE ANALYSIS: The samples were analyzed by gas chromatograph (GC) with a flame ionization detector (FID). The GC was set up with an autosampler and a 30-m x 0.25-mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and detector at 320ºC. The autosampler was set to inject 1 µL of the matrix dilution.

Data Quality Objectives	**Control Limits**
Procedural Blank	< 5 X MDL
Blank Spike Recovery	40% – 120%
Continuing Standard Recovery	75% – 125%

QA/QC SUMMARY

METHODS: GC-FID

CALIBRATION: Calibration with a five-point curve was done using standards EDSP Mix 1 (see Appendix C) with a continuing calibration verification (CCV) sample analyzed every 10 samples.

CONTINUING STANDARD Percent recovery results for initial and CCV samples analyzed with the in-life

RECOVERY: sample data set ranged from 92% to 116% with a mean recovery of 100%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK: Atrazine was not detected above the detection limit in the corn oil blank analyzed with the test solution and in-life samples.

DETECTION LIMIT: The atrazine detection limit in corn oil was 115 µg/mL as determined by an MDL study. No data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed. In this analysis, sampling was performed by taking the sample material from flask through to analysis. Analyzing a spiked sample would be no different from analyzing a CCV.

INTERNAL STANDARD: 5a androstane was spiked into each sample and analyzed as the internal standard. Average percent recovery results were 96% and ranged from 79% to 111%. There were no cases in which the percent recovery of the internal standard exceeded the acceptance range of 40% to 120%.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSDs) for the two test solutions prepared for female exposures ranged from 1.27 to 3.25.

The % RSDs for formulations prepared for exposure to males ranged from 0.673 to 2.33.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of Atrazine Concentrations in Formulations Prepared 09/09/02 for Female Exposures

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	%RSD
15 mg/mL	2-14 –D-F Top R-1, R-1	14.2		
15 mg/mL	2-14 –D-F Top R-1, R-2	13.9	14.0	1.27
15 mg/mL	2-14 –D-F Top R-1, R-3	13.8		
15 mg/mL	2-14 –D-F Bott R-1, R-1	14.6		
15 mg/mL	2-14 –D-F Bott R-1, R-2	13.9	14.2	2.74
15 mg/mL	2-14 –D-F Bott R-1, R-3	14.0		
30 mg/mL	2-14 –E-F Top R-1, R-1	26.9		
30 mg/mL	2-14 –E-F Top R-1, R-2	28.2	27.9	3.06
30 mg/mL	2-14 –E-F Top R-1, R-3	28.6		
30 mg/mL	2-14 –E-F Bott R-1, R-1	29.1		
30 mg/mL	2-14 –E-F Bott R-1, R-2	28.3	28.2	3.25
30 mg/mL	2-14 –E-F Bott R-1, R-3	27.3		

Table 2. Verification of Atrazine Concentrations in Formulation Prepared on 09/25/02 and 10/02/02 for Male Exposures

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	%RSD
09/25/02				
15 mg/mL	2-14 –Q-M Top R-1, R-1	13.7		
15 mg/mL	2-14 –Q-M Top R-1, R-2	14.1	13.8	2.33
15 mg/mL	2-14 –Q-M Top R-1, R-3	13.5		
15 mg/mL	2-14 –Q-M Bott R-1, R1	13.9		
15 mg/mL	2-14 –Q-M Bott R-1, R-2	13.8	14.0	1.70
15 mg/mL	2-14 –Q-M Bott R-1, R-3	14.3		
30 mg/mL	2-14 –R-M Top R-1, R-1	27.5		
30 mg/mL	2-14 –R-M Top R-1, R-2	28.6	28.3	2.31
30 mg/mL	2-14 –R-M Top R-1, R-3	28.7		
30 mg/mL	2-14 –R-M Bott R-1, R-1	28.6		
30 mg/mL	2-14 –R-M Bott R-1, R-2	29.3	29.0	1.17
30 mg/mL	2-14 –R-M Bott R-1, R-3	29.0		
10/02/02				
15 mg/mL	2-14-Q-M R-2, R-1	15.7		
15 mg/mL	2-14-Q-M R-2, R-2	15.9	15.8	0.673
15 mg/mL	2-14-Q-M R-2, R-3	15.7		
30 mg/mL	2-14-R-M R-2, R-1	30.7		
30 mg/mL	2-14-R-M R-2, R-2	30.7	30.6	0.771
30 mg/mL	2-14-R-M R-2, R-3	30.3		

Table 3. In-life Sample Atrazine – Females

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
09/18/02	10/16/02	6/4/03	15 mg/mL	WA2-14D-F 9-18 Vial	16.77	112%
09/24/02	10/16/02	6/4/03	15 mg/mL	WA2-14D-F 9-24 Vial	16.93	113%
10/01/02	10/16/02	6/4/03	15 mg/mL	WA2-14D-F 10-1 Vial	16.90	113%
10/08/02	10/16/02	6/4/03	15 mg/mL	WA2-14D-F 10-8 Vial	16.44	110%
09/18/02	10/16/02	6/4/03	30 mg/mL	WA2-14E-F 9-18 Vial	33.63	112%
09/24/02	10/16/02	6/4/03	30 mg/mL	WA2-14E-F 9-24 Vial	32.95	110%
10/01/02	10/16/02	6/4/03	30 mg/mL	WA2-14E-F 10-1 Vial	33.28	111%
10/08/02	10/16/02	6/4/03	30 mg/mL	WA2-14E-F 10-8 Vial	33.11	110%

Table 4. In-life Sample Atrazine - Males

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
10/07/02	11/13/02	06/05/03	15 mg/mL	WA2-14Q-M 10-7 Vial	17.15	114%
10/14/02	11/13/02	06/05/03	15 mg/mL	WA2-14Q-M 10-14Vial	16.81	112%
10/21/02	11/13/02	06/05/03	15 mg/mL	WA2-14Q-M 10-21Vial	16.85	112%
10/28/02	11/13/02	06/05/03	15 mg/mL	WA2-14Q-M 10-28Vial	17.02	113%
10/07/02	11/13/02	06/05/03	30 mg/mL	WA2-14R-M 10-7 Vial	33.80	113%
10/14/02	11/13/02	06/05/03	30 mg/mL	WA2-14R-M 10-14Vial	33.10	110%
10/21/02	11/13/02	06/05/03	30 mg/mL	WA2-14R-M 10-21Vial	31.43	105%
10/28/02	11/13/02	06/05/03	30 mg/mL	WA2-14R-M 10-28Vial	32.11	107%

Table 5. Post-Test Atrazine Concentrations in Formulations Returned to Battelle

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
Female Exposures						
09/15/02	10/16/02	11/22/02	15 mg/mL	WA 2-14-D-F Rep2Jar	14.0	93%
09/15/02	10/16/02	11/22/02	30 mg/mL	WA 2-14-E-F Rep2Jar	27.8	93%
Male Exposures						
10/2/02	11/13/02	11/22/02	15 mg/mL	WA 2-14-Q-M Rep3Jar	14.1	94%
10/2/02	11/13/02	11/22/02	30 mg/mL	WA 2-14-R-M Rep3Jar	28.8	96%

Deviation Documentation Form

Project No. EDSP WA 2-14/ atrazine
Deviation No. WA 2-14-D-002
Project Manager: Eric Crecelius

EDSP WA 2-14 and The EDSP Chemical Repository

Entered by: Lohna O'Rourke Date: 2/12/03

The following information is (check one)
[x] a miscellaneous documentation
[ ] a deviation from Protocol, Work Plan or QA Plan (give title)

-

[ ] a deviation from SOP
(give number and title)

Description: According to LRB 009 three lots of atrazine were used in the preparation of the formulations. All lots were analyzed by Battelle for purity and were determined to be 98% or greater. However, the chemical inventory records book is not in agreement with the quantity of chemical remaining for each lot.

Corrective Action: No corrective action.

Action to Prevent Recurrence: Staffs that work in the Chemical Repository have received additional training on maintaining the chemical inventory records.

Impact on Project: No impact to the project. Both lots were analyzed and had purities of 98% or greater.

APPROVED BY: Eric Crecelius 2/12/03

Eric Crecelius, Study Manager
Chemical Repository

Date

File in project notebook or study archive
Send a copy to the MSL QA Officer

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-004: Atrazine, DDE, vinclozolin, Methoxychlor, Fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[X]	Protocol
[ ]	SOP	[ ]	Method	[ ]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: 2.3 of protocol WA 2-14 states "an aliquot of each level per formulation will be analyzed"

DEVIATION: Each dose level was tested in the first preparation for each chemical. However, subsequent batches were not always analyzed.

REASON/IMPACT: No impact. Subsequent batches were prepared using the same methods and procedures as the first batches.
PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action required.

ACTIONS TO PREVENT RECURRENCE: Upper management will review the analyses schedule prior to the start of the studies.

Approval:

Michael Blanton,
WAL — Date 11-3-03

Eric Crecelius,
Study Director
Chemical Repository — Date 11-3-03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Bisphenol A in Mazola Corn Oil

November 3, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory

1529 West Sequim Bay Road

Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology

Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Bisphenol A in Mazola Corn Oil

Reviewed by: _____

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Bisphenol A in Mazola Corn Oil

Parameter	Chemical
Compound Name	Bisphenol A
CAS #	80-05-7
Central File No.	CF-1825
Receipt Date	10/15/2002
Expiration Date	10/2004
Manufacturer	Fisher Scientific
Lot Number	A0147444
Battelle Study #	WA2-14-02-02
Method	SW 846, 8316 Modified

Executive Summary

The chemical purity of Bisphenol A determined by the manufacturer was 99.6%. The purity result from Battelle-Sequim by HPLC was determined to be 100.00%. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of Bisphenol A was expected to stay greater than or equal to 90% of the target concentration for up to 12 weeks. Thus, stability testing of the Bisphenol A stock solution in Mazola corn oil was considered stable at 80 mg/mL for the required testing and holding period of 12 weeks.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries based on target concentrations for all doses ranged from 99% to 112%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA2-14-02-02, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of Bisphenol A (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_BisphenolA-cornoil.doc, PSTP_WA-2-14_BisphenolA-cornoil.doc, DSUM_WA2-14_BisphenolA-crnoil.xls, and DAF_WA-2-14_BisphenolA-cornoil.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, Bisphenol A, (CAS No. 80-05-7) was purchased for purity and stability analysis to support a pubertal study on rats (Figure 1). Bisphenol A was purchased from Fisher Scientific and lot number A0147444 was received on 10/15/2002 with an expiration date of 10/2004 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1825) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-02

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Bisphenol A (MSL CF 1825)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 80 mg/mL and 120 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Planned/proposed testing/holding duration: 12 weeks

Chemical Information

Chemical Name: Bisphenol A

CAS: 80-05-7

Any known purity information: may refer to attached documentation

Manufacturer's Purity Information: 99.6% pure

Any known stability information: may refer to attached documentation

Manufacturer's Stability Information: stable

Desired purity (%) for test? 95% or greater

Figure 1. EDSP Requisition Form for Bisphenol A

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Bisphenol A
CAS #	80-05-7
Central File No.	CF-1825
Receipt Date	10/15/2002
Expiration Date	10/2004
Manufacturer	Fisher Scientific
Lot Number	A0147444
Manufacturer's Purity	99.6%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA2-14-02-02
Method	SW 846, 8316 Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak, and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted using high performance liquid chromatograph (HPLC) with ultraviolet (UV) absorbance at 275 nm by making a solution of 1 mL of the stock solution and diluting it with 9 mL of a 60% acetonitrile (ACN): 40% de-ionized water solution. This matrix was then run on the HPLC and the purity determined by comparing the peak heights of the peaks in the chromatogram. The HPLC was set up with an auto sampler and a column oven. The column oven temperature was set at 30ºC, and the auto sampler was set to inject 250 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. A single stock solution was prepared to arrive at the 80 mg/mL concentration requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

A Bisphenol A stock matrix was prepared on 10/17/02 for testing as described in Table 2. The first analysis was done 10/18/02; this was considered the start of the test. Briefly, to prepare the 80 mg/mL Bisphenol A concentration, 16.0 g of Bisphenol A was weighed into a 250 mL amber glass wide mouth jar containing 170 g of corn oil, a stir bar was added, and the solution was mixed on a stir plate over night to suspend the chemical. The stock was transferred to an ashed, amber glass bottle, labeled, and stored at 4ºC ± 2ºC for the duration of the test.

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA2-14-02-02 12 Weeks	Bisphenol A	80 mg/mL	1825-1a-2	16.0 g in 170 g Mazola corn oil

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the stock concentration was determined by chromatographic analysis. Triplicate aliquots of each concentration were tested. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

The samples were analyzed using an HPLC with an ultraviolet/visible (UV/VIS) detector at the 275 nm wavelength. A 60:40% ACN:water mix was used for the eluent at 1.5 mL/minute. Separation was attained using a Supelco PAH (25 cm x 4.8 mm, C-18 column). Calibrations were performed using dilutions prepared from standard PP-1190. For samples analyzed using the HPLC system, data are stored in MSL5, room 219 on the computer with a property number of WV04738.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a HPLC purity scan on the Bisphenol A. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for Bisphenol A and several very small peaks. The area of the Bisphenol A peak was 100.00% of the total area of all peaks in the chromatogram. Chemical purity of Bisphenol A as determined by the manufacturer was 99.6% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 10/18/02. Chemical concentration was determined 10 times from 10/18/02 to 01/08/03. The analytical and quality control (QC) results are presented in Appendix C. A single preparation blank was analyzed with every batch for quality control purposes. There were no detectable concentrations of Bisphenol A in the blanks. CCV results ranged from 89.2% to 107%. Internal standards were not run. The MDL was 500,000 ng/mL or 0.5 mg/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg as required for biological testing (Appendix C). The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively.

3.3 Statistical Results of Stability Trial

A plot of Bisphenol A with a target concentration of 80,000,000 ng/mL against time suggests virtually no chemical decay (Figure 2). Homogeneity of the top and bottom concentrations of Bisphenol A in the testing container was tested at time 0. Concentrations in the bottom of the container averaged 87406525 ng/mL with a standard deviation of 526768. Concentrations in the top of the container averaged 85362947 ng/mL with a standard deviation of 1436907. Although the bottom concentration was greater than the top, there was not enough power to reject the null hypothesis that the average concentrations were the same. For the final regression model, the three bottom samples were removed from the analysis. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of Bisphenol A was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 12 weeks (Table 3). Thus, this stock solution was considered stable for the required 12-week testing/holding period. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses ranged from 99% to 112%. The complete analysis is presented in Appendix E.

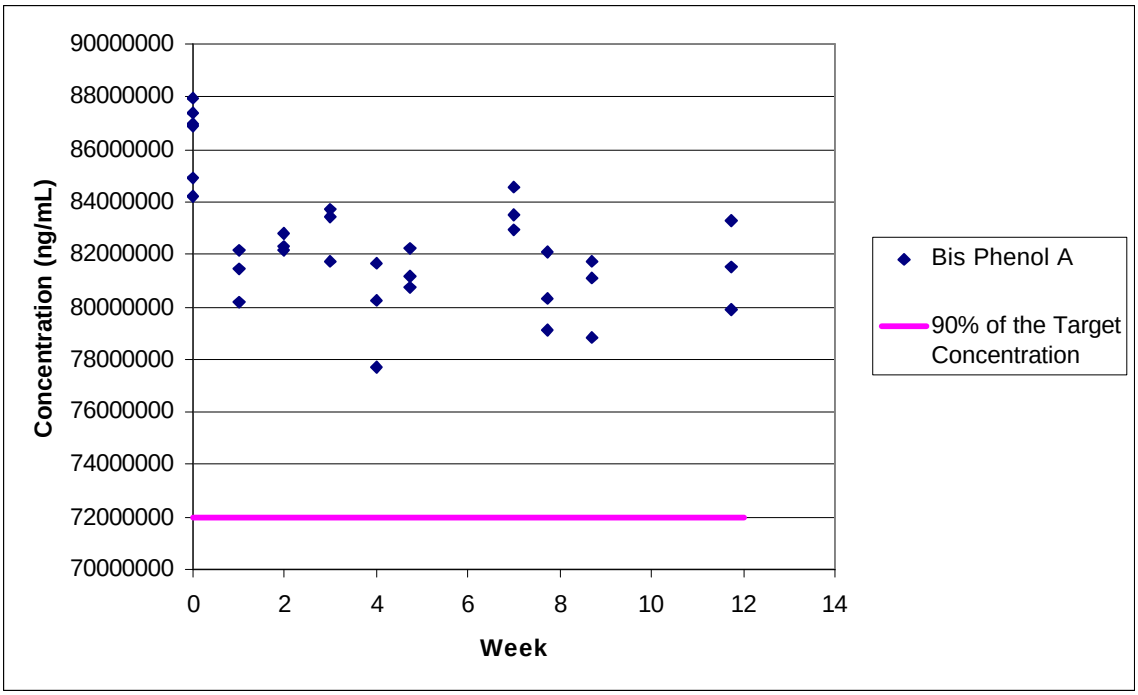

Figure 2. Observed Concentration of Bisphenol A with a Target Concentration of 80,000,000 ng/mL Against Time

Table 3. Summary of Statistical Results for Bisphenol A

WA-2-14-02-02 **Statistical Analysis conducted by Valerie Cullinan** **Using Minitab Version 13.32, Minitab Inc., 1999.**	**1825-1a-2** **Bisphenol A**
Target Concentration (ng/mL)	80000000
Number of determinations	1
Number of weeks tested	12
Number of replicates per day	3
Number of outliers removed	0
Number of observations removed	3 [a]
Overall Mean Concentration	82450509
95% Upper CL	83172788
error degrees of freedom	32
1-sample t-test of Ho: μ >= Target	NS [b]
Estimated intercept of ln(concentration) against time	18.2329
Estimated slope of ln(concentration) against time	-0.0022
standard error of slope	0.0011
error degrees of freedom	28
Significance test of lack-of-fit for final model	S [c]
Significance test of Ho: $\beta = 0$ vs. H1: $\beta = 0$	NS
Lower 95% CL	-0.005
Upper 95% CL	0.000
Maximum Percent Loss (using LCL)	3.6%
Mean Percent Loss (using bhat)	1.8%
LN(90% of Target)	18.0922
Number of weeks until at 90% of Target (using LCL)	31
Conclusion:	**Stable for 12 wks**

[a] Removed for regression only

[b] Not Significant at a = 0.05

[c] Significant at a = 0.05

4.0 CONCLUSIONS

Chemical purity of Bisphenol A determined by the manufacturer was 99.6%; purity determined by Battelle-Sequim was 100%. Stability testing of Bisphenol A in Mazola corn oil concluded that the chemical was stable at the 80 mg/mL concentration for a period of 12 weeks.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses ranged from 99% to 112%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

CERTIFICATE OF ANALYSIS

Product 15824-0000

4,4'-ISOPROPYLIDENEDIPHENOL, 97%

Specifications	
Appearance	White prills
Infrared spectrometry	AUTHENTIC
Melting point	155°C to 158°C
Separat. techn. GC	>98.0 %

General Product Data

Version	00
CAS No	80-05-7
Molecular weight	228.29
Molecular formula	C15 H16 O2
Linear formula	(CH3)2C(C6H4OH)2
Flash point (°C)	227

Lot Specific Data **Lot No. A0147444**

Appearance	**White prills**
Infrared spectrometry	**authentic**
Melting point	**157.3°C**
Separat. techn. GC	**99.6 %**

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Issued: 20/11/01
A. Vanneste Quality Control Manager
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2000 Park Lane Drive, Pittsburgh, PA 15275-1126, USA *Tel:1-800-766-7000 *Fax:1-800-926-11-66 *Internet: http://www.fisherscientific.com

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Bisphenol A

Chemical Name: Bisphenol A (MSL CF 1825), CMS 173720

CAS Number: 80-05-7

Lot Number: A0147444, stored at RT in MSL5, Rm 219

Expiration date: 10/2004

Manufacturer's Purity Information: 99.6%

Manufacturer's Stability Information: stable

MSL Purity Results:
Purity (%) To be determined at MSL by LC scan

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Bisphenol A

CAS: 80-05-7

Carrier(s): suspended in Mazola corn oil

Concentrations/Dilution Series: 80 mg/mL and 120 mg/mL

Below MDL determined in Purity Analysis?

In vitro or in *vivo tests*? *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Planned/Proposed testing/holding duration: 12 weeks

Design of Stability Test: One concentration of Bisphenol A, 80 mg/mL in Mazola corn oil, will be tested. The chemical will be sieved through an 80 mesh screen and material that passes will be suspended in Mazola corn oil with a magnetic stirrer. Samples of the suspension will be taken with a gavage needle, while the suspension is being vigorously stirred, at mid-depth in a 250 mL amber glass bottle, except for the first sampling, which will be sampled at 25% and 75% depth in triplicate to demonstrate homogeneity. The suspension will be stored in glass at 4 deg. C in the dark for 12 weeks, sampled at least 8 times in triplicate and analyzed monthly by LC.

Number of replicates: 3

Duration: 12 weeks, sampling at least 8 time points with triplicate samples taken each time

Other factors:
Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other: None

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:
Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
  - Chemical repository confirmatory test results of chemical identity and purity;
  - Chemical repository test results of lot-to-lot variation in chemical purity;
  - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- Dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. Bisphenol A concentration in Mazola Corn Oil (ng/mL)

Target Concentration.	Sample ID	Date	Bisphenol A	Average	RSD	Recovery[b]
80000000	1825-1a-2-1 Top R-1[a]	10/18/02	84187864			
80000000	1825-1a-2-1 Top R-2[a]	10/18/02	86964928	85362947	1.68%	107%
80000000	1825-1a-2-1 Top R-3[a]	10/18/02	84936048			
80000000	1825-1a-2-1 Bottom R-1[a]	10/18/02	87954672			
80000000	1825-1a-2-1 Bottom R-2[a]	10/18/02	87360784	87406525	0.60%	109%
80000000	1825-1a-2-1 Bottom R-3[a]	10/18/02	86904120			
Blank	1825-1a-2-1 Blank1	10/18/02	500000 U			
80000000	1825-1a-2-2 R-1	10/25/02	82182592			
80000000	1825-1a-2-2 R-2	10/25/02	81433368	81255619	1.26%	102%
80000000	1825-1a-2-2 R-3	10/25/02	80150896			
Blank	1825-1a-2-2 Blank2	10/25/02	500000 U			
80000000	1825-1a-2-3 R-1	11/1/02	82178864			
80000000	1825-1a-2-3 R-2	11/1/02	82765736	82418317	0.37%	103%
80000000	1825-1a-2-3 R-3	11/1/02	82310352			
Blank	1825-1a-2-2 Blank3	11/1/02	500000 U			
80000000	1825-1a-2-4 R-1	11/8/02	83436800			
80000000	1825-1a-2-4 R-2	11/8/02	81713344	82949379	1.30%	104%
80000000	1825-1a-2-4 R-3	11/8/02	83697992			
Blank	1825-1a-2-2 Blank4	11/8/02	500000 U			
80000000	1825-1a-2-5 R-1	11/15/02	80263496			
80000000	1825-1a-2-5 R-2	11/15/02	81660944	79866467	2.53%	99.8%
80000000	1825-1a-2-5 R-3	11/15/02	77674960			
Blank	1825-1a-2-2 Blank5	11/15/02	500000 U			
80000000	1825-1a-2-6 R-1	11/20/02	80763600			
80000000	1825-1a-2-6 R-2	11/20/02	81146368	81383843	0.94%	102%
80000000	1825-1a-2-6 R-3	11/20/02	82241560			
Blank	1825-1a-2-2 Blank6	11/20/02	500000 U			
80000000	1825-1a-2-7 R-1	12/6/02	83523000			
80000000	1825-1a-2-7 R-2	12/6/02	84591336	83685379	1.00%	105%
80000000	1825-1a-2-7 R-3	12/6/02	82941800			
Blank	1825-1a-2-2 Blank7	12/6/02	500000 U			
80000000	1825-1a-2-8 R-1	12/11/02	79119720			
80000000	1825-1a-2-8 R-2	12/11/02	80287136	80500971	1.86%	101%
80000000	1825-1a-2-8 R-3	12/11/02	82096056			
Blank	1825-1a-2-2 Blank8	12/11/02	500000 U			
80000000	1825-1a-2-9 R-1	12/18/02	81761024			
80000000	1825-1a-2-9 R-2	12/18/02	81071256	80543776	1.92%	101%
80000000	1825-1a-2-9 R-3	12/18/02	78799048			
Blank	1825-1a-2-2 Blank9	1218/02	500000 U			
80000000	1825-1a-2-10 R-1	01/8/03	79886664			
80000000	1825-1a-2-10 R-2	01/8/03	81546472	81582376	2.10%	102%
80000000	1825-1a-2-10 R-3	01/8/03	83313992			
Blank	1825-1a-2-2 Blank10	1/8/03	500000 U			

[a] Time 0 samples collected from top and bottom of container to assess homogeneity

[b] Recovery is relative to the target concentration

U = Not detected at a value greater than the MDL

Table C.2. CCV Data for Bisphenol A Concentration in Mazola Corn Oil

Time	Sample Name	Bisphenol A (µg/L)	Recovery	PD
-	Bis 500 PP-1190C	470.83	94.17%	5.83%
-	Bis 500 PP-1190C	508.41	101.68%	1.68%
-	Bis 500 PP-1190C	488.62	97.72%	2.28%
-	Bis 500 PP-1190C	469.30	93.86%	6.14%
-	Bis 500 PP-1190C	494.70	98.94%	1.06%
-	Bis 500 PP-1190C	486.65	97.33%	2.67%
-	Bis 500 PP-1190C	499.71	99.94%	0.06%
-	Bis 500 PP-1190C	487.66	97.53%	2.47%
-	Bis 500 PP-1190C	485.70	97.14%	2.86%
-	Bis 500 PP-1190C	447.91	89.58%	10.42%
-	Bis 500 PP-1190C	445.92	89.18%	10.82%
-	Bis 500 PP-1190C	507.29	101.46%	1.46%
-	Bis 500 PP-1190C	495.77	99.15%	0.85%
-	Bis 500 PP-1190C	497.27	99.45%	0.55%
-	Bis 500 PP-1190C	535.30	107.06%	7.06%
-	Bis 500 PP-1190C	493.11	98.62%	1.38%
-	Bis 500 PP-1190C	489.18	97.84%	2.16%
-	Bis 500 PP-1190C	482.24	96.45%	3.55%
-	Bis 500 PP-1190C	494.87	98.97%	1.03%
-	Bis 500 PP-1190C	507.29	101.46%	1.46%
-	Bis 500 PP-1190C	495.77	99.15%	0.85%

Table C.3. Internal Standards Data for Bisphenol A in Mazola Corn Oil

Sample Name	Date	5A Androstane Recovery

Not applicable

Table C.4. Peroxide Concentration in Mazola Corn Oil (meq/kg)

Sample	Analysis Date	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	09/05/02	0.5	0.005	5.00	0.50		
Mazola Corn Oil Expiration 6-03 R-1	09/05/02	1.9	0.005	5.01	1.90		
Mazola Corn Oil Expiration 6-03 R-2	09/05/02	1.8	0.005	5.36	1.68	1.77	6.41
Mazola Corn Oil Expiration 6-03 R-3	09/05/02	1.8	0.005	5.16	1.74		
Mazola Corn Oil Expiration 1-04 R-1	09/05/02	1.2	0.005	4.92	1.22		
Mazola Corn Oil Expiration 1-04 R-2	09/05/02	1.5	0.005	5.2	1.44	1.34	8.31
Mazola Corn Oil Expiration 1-04 R-3	09/05/02	1.4	0.005	5.13	1.36		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-02
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

5/23/2003 12:40:38 PM

Results for: Week 0

Two-Sample T-Test and CI: Bisphenol A, section

Two-sample T for Bisphenol A

section	N	Mean	StDev	SE Mean
1	3	87406525	526768	304129
2	3	85362947	1436907	829599

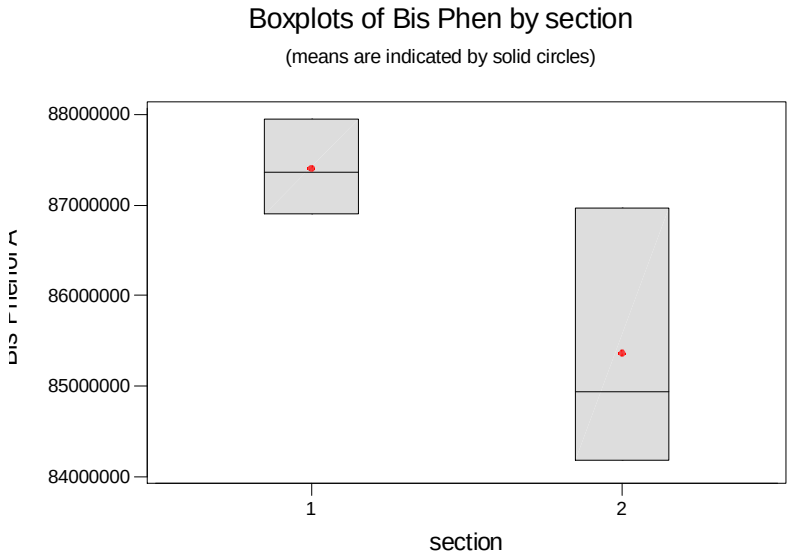
1 = bottom

2 = top

Very poor power!

Difference = mu (1) - mu (2)
Estimate for difference: 2043579
95% CI for difference: (-1758197, 5845354)
T-Test of difference = 0 (vs not =): T-Value = 2.31 P-Value = 0.147 DF = 2

NS



Kruskal-Wallis Test: Bisphenol A versus section

Kruskal-Wallis Test on Bisphenol

section	N	Median	Ave Rank	Z
1	3	87360784	4.7	1.53
2	3	84936048	2.3	-1.53
Overall	6		3.5	

H = 2.33 DF = 1 P = 0.127 NS
* NOTE * One or more small samples

Conclusion: For the week 0 data, the test between sections has very poor power, note the width of the 95% CI of the difference (-1758197, 5845354). Because one sample from the top section was about the same concentration as one sample of the bottom section, no difference could be detected.

Results for: Stability Data

- Performs a one-sample t-test for mu less than TARGET &

What is the target value for X 3
DATA> 80000000

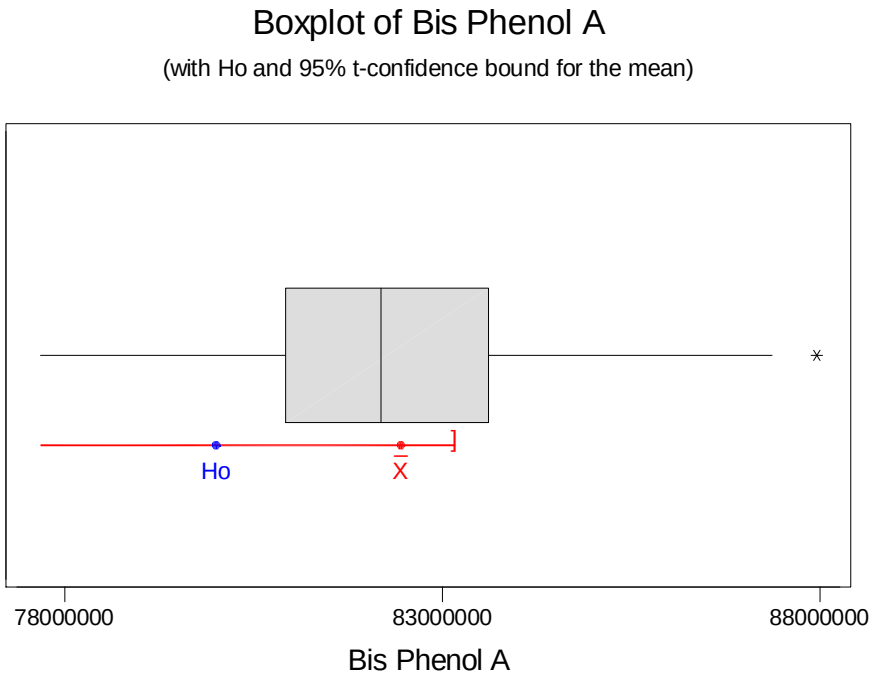
One-Sample T: Bisphenol A

Test of mu = 80000000 vs mu < 80000000

Variable	N	Mean	StDev	SE Mean
Bisphenol A	33	82450509	2449500	426403

Variable	95.0% Upper Bound	T	P
Bisphenol A	83172788	5.75	1.000

NS



- Outliers are < Median-3*IQD OR > Median+3*IQD

Boundary for outliers are values < 74099660 and > 90258068

No outliers

- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	18.2486
0	2	18.2810
0	3	18.2574
0	1	18.2923
0	2	18.2856
0	3	18.2803
1	1	18.2245
1	2	18.2153
1	3	18.1994
2	1	18.2244
2	2	18.2315
2	3	18.2260
3	1	18.2396
3	2	18.2187
3	3	18.2427
4	1	18.2008
4	2	18.2181
4	3	18.1680
5	1	18.2070
5	2	18.2118
5	3	18.2252
7	1	18.2406
7	2	18.2533
7	3	18.2336
8	1	18.1865
8	2	18.2011
8	3	18.2234
9	1	18.2193
9	2	18.2108
9	3	18.1824
12	1	18.1961
12	2	18.2167
12	3	18.2381

- Conducts Simple Linear Regression

Regression Analysis: Bisphenol A versus Week

The regression equation is
Bisphenol A = 18.2 - 0.00382 Week

Predictor	Coef	SE Coef	T	P
Constant	18.2450	0.0072	2541.21	0.000
Week	-0.003822	0.001201	-3.18	0.003

S = 0.02603 R-Sq = 24.6% R-Sq(adj) = 22.2%

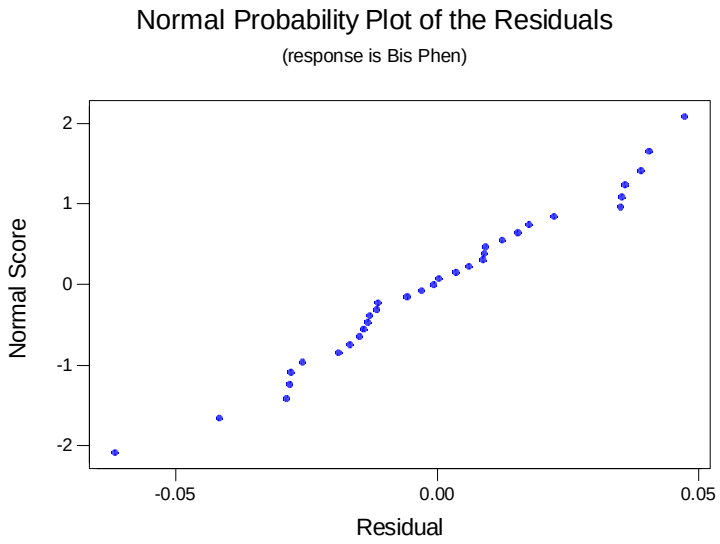
Analysis of Variance

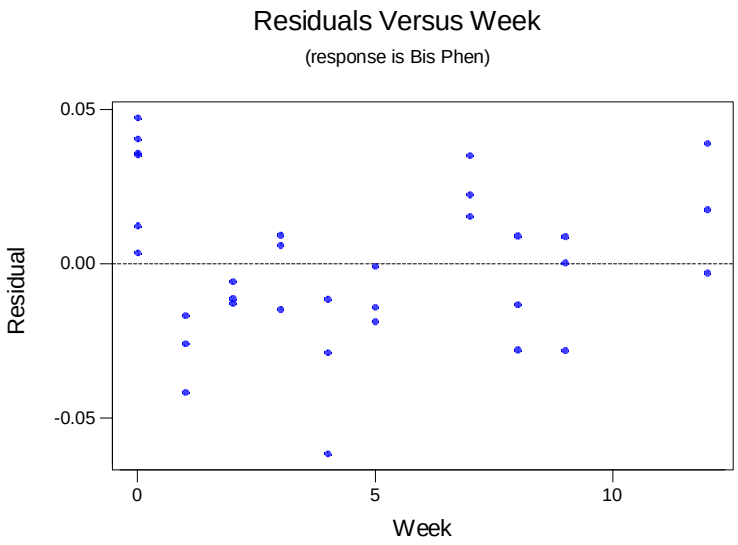
Source	DF	SS	MS	F	P
Regression	1	0.0068616	0.0068616	10.13	0.003
Residual Error	31	0.0210054	0.0006776		
Lack of Fit	8	0.0148455	0.0018557	6.93	0.000
Pure Error	23	0.0061598	0.0002678		
Total	32	0.0278670			

Unusual Observations

Obs	Week	Bisphen	Fit	SE Fit	Residual	St Resid
18	4.0	18.1680	18.2297	0.0046	-0.0617	-2.41R

R denotes an observation with a large standardized residual





Do you want to remove any data points? (yes OR no)
no

Should a quadratic be fit? (yes OR no)
No

- Power analysis for t-test of slope less than zero

Power and Sample Size

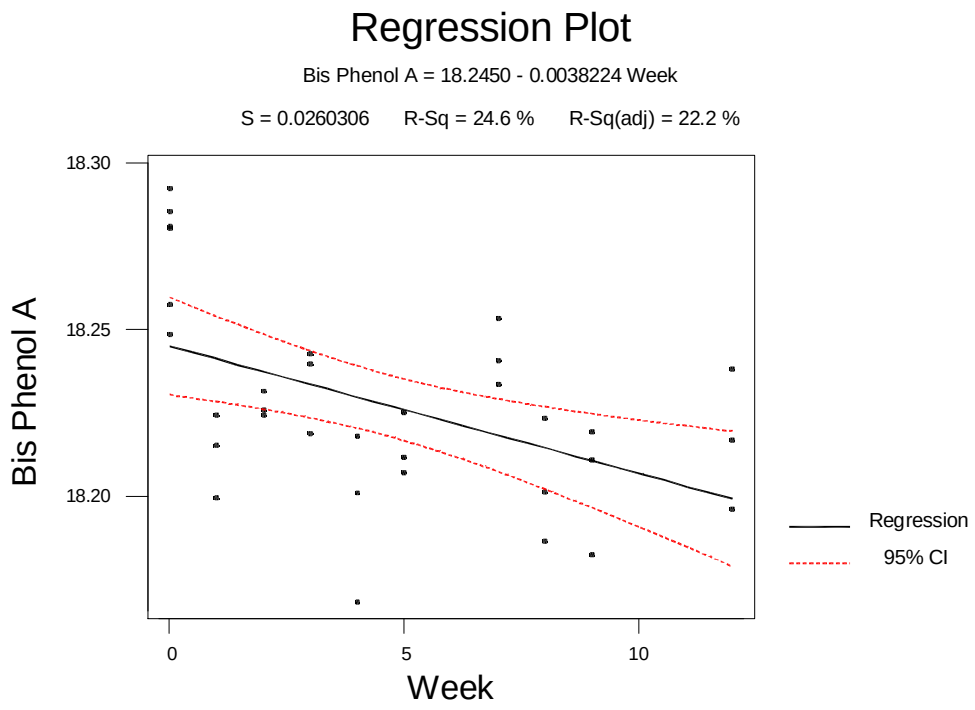
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05 Sigma = 0.0260306

Sample
  Size   Power Difference
    31 0.9900   -0.0190

- That means we would detect a mean of 18.178 as significantly less than ln(80000000) = 18.198 or a change of 78494349 from 80000000 = 1.9% loss.

- Fit 95% confidence bands about the fitted simple linear model



- Remove the three bottom samples from Week 0 from the analysis

Regression Analysis: Bisphenol A versus Week

The regression equation is
Bisphenol A = 18.2 - 0.00225 Week
30 cases used 3 cases contain missing values

Predictor	Coef	SE Coef	T	P
Constant	18.2329	0.0071	2562.71	0.000
Week	-0.002247	0.001135	-1.98	0.058

S = 0.02266 R-Sq = 12.3% R-Sq(adj) = 9.1%

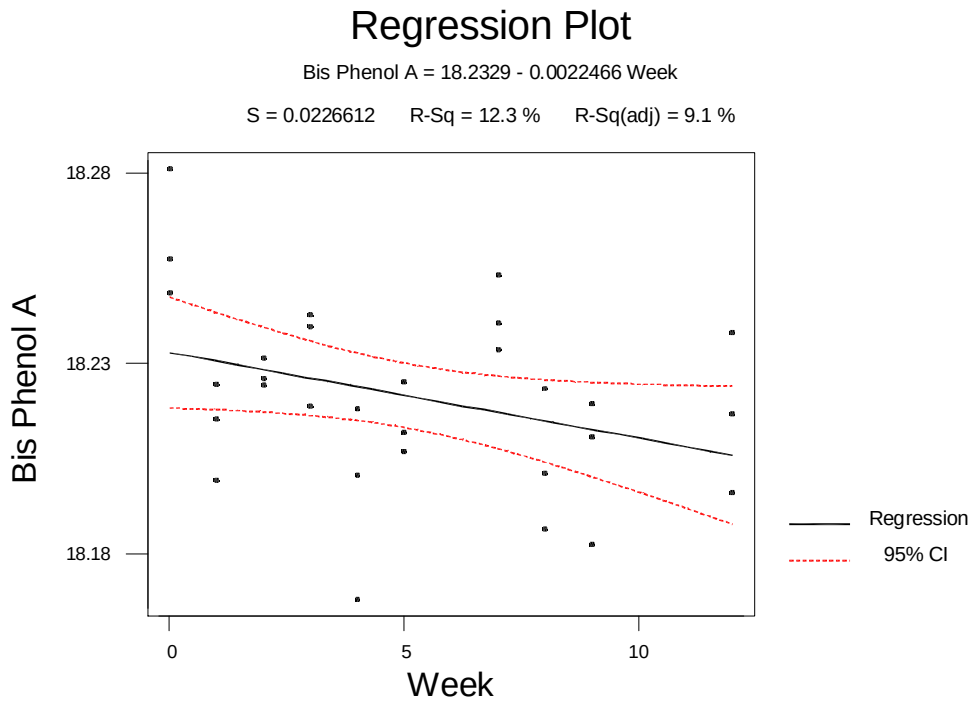
Analysis of Variance

Source	DF	SS	MS	F	P	
Regression	1	0.0020124	0.0020124	3.92	0.058	
Residual Error	28	0.0143788	0.0005135			
Lack of Fit	8	0.0091369	0.0011421	4.36	0.004	**
Pure Error	20	0.0052419	0.0002621			
Total	29	0.0163912				

Unusual Observations

Obs	Week	Bisphenol	Fit	SE Fit	Residual	St Resid
2	0.0	18.2810	18.2329	0.0071	0.0482	2.24R
18	4.0	18.1680	18.2239	0.0043	-0.0558	-2.51R

R denotes an observation with a large standardized residual



- **Conclusion – stable for 12 weeks.**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Bisphenol A in-life test solution samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Bisphenol A suspended in corn oil

TEST SOLUTION SAMPLE CUSTODY AND PROCESSING:

Test solution samples were prepared by the EDSP Chemical Repository, Sequim, WA, using Bisphenol A (CF 1825, Fisher Acros lot # A0147444, expiration date 10/04) suspended in Mazola corn oil (corn oil was from containers with the following expiration dates: 06/12/03, 01/01/04, and 04/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time. Two test solutions at each of the test concentrations were prepared at one time on 11/20/02 and shipped on two different dates, 11/21/02 (Rep 1) and 11/25/02 (Rep 2). Samples were prepared at two test concentrations: 80 mg/mL and 120 mg/mL. The 80 mg/mL concentration was prepared by adding 16.0 g of Bisphenol A in 170 g of corn oil in a pre-cleaned, amber glass container. The 120 mg/mL concentration was prepared by adding 24.0 g of Bisphenol A in 162 g of corn oil. Bisphenol A was sieved through an 80-mesh, stainless-steel screen prior to weighing. Stir bars were added to aid in mixing to keep the chemical in suspension. The samples were analyzed on 11/20/02 to verify concentrations prior to shipping (Table 1).

The test solution was sampled four times during the test on 11/27/02, 12/3/02, 12/10/02, and 12/17/02, for each of the two test concentrations with no replication. These samples were returned in scintillation vials at the conclusion of the test. Empty containers with trace amounts of chemical, containers with remaining chemical volumes (from 140 mL to 190 mL), and scintillation vials with in-life samples were returned for analysis. These samples were received from RTI on 12/20/02. Empty containers with trace amounts of chemical were not analyzed. Two containers with remaining chemical volumes were analyzed and labeled "remain."

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:

The container was placed on a magnetic stir plate and stirred. 1 mL triplicate samples were removed and each placed in a tared, 120 mL amber glass bottle. The weight of the sample was determined gravimetrically. 100 mL of acetonitrile (ACN) was added and the bottle agitated to mix. For the 80 mg/mL concentration, 0.01 mL was then transferred to an auto sampler vial with 0.99 mL of 60% ACN in water. For the 120 mg/mL concentration, 0.005 mL was then transferred to an auto sampler vial with 0.995 mL of 60% ACN in water.

In-life and Returned Container Samples:

For the containers with sufficient material to analyze, the containers were removed from the refrigerator, allowed to warm to room temperature, and then stirred using a magnetic stir bar and stir plate. About 1 mL was sampled and placed in a tared, 120 mL, amber glass bottle. The weight of the sample was determined gravimetrically. Some of the containers contained a slurry with Bisphenol A settled to the bottom. The entire sample was extracted to ensure accurate analysis. For the smaller scintillation vial samples, the vial was weighed, the contents poured into 20 mL, amber glass bottle, and the vial rinsed with part of the 100 mL ACN to be used, ensuring that the vials were rinsed as completely as possible to recover all of the chemical. The amber bottles were agitated to mix, and 0.1 mL transferred to an auto sampler vial with 0.9 mL ACN. Then 0.01 mL was transferred to another auto sampler vial with 0.99 mL 60% ACN in water. For the "remainder" sample, 0.01 mL was transferred to an auto sampler vial with 0.99 mL 60% ACN:water mixture, and then 0.005 mL transferred to a vial with 0.995 mL ACN:water.

SAMPLE ANALYSIS: The samples were analyzed using a high performance liquid chromatograph (HPLC) with an ultraviolet/visible (UV/VIS) detector at the 275-nm wavelength. A 60:40% ACN:water mix was used for the eluent at 1.5 mL/minute. Separation was attained using a Supelco PAH (25 cm x 4.8 mm, C-18) column. Calibrations were performed using dilutions prepared from standard PP-1190. For samples analyzed using the HPLC system, data are stored in MSL5, room 219 on the computer with a property number of WV04738.

Data Quality Objectives	**Control Limits**
Procedural Blank	<5 X MDL
Blank Spike Recovery	40% - 120%
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: HPLC with a UV/VIS detector at the 275 nm wavelength.

CALIBRATION: Calibration with a five-point curve was done using standards prepared from dilutions of PP-1190 (curve from 10/17/02) and a continuing calibration verification (CCV) samples analyzed every 10 samples. Although a calibration series was run with each sample run to assess drift or change in the curve, the 10/17/02 calibration curve was used.

CONTINUING STANDARD RECOVERY: Percent recovery results for four CCV samples analyzed with the in-life sample data set ranged from 89% to 99%, with a mean recovery of 96%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK: Bisphenol A was not detected above the detection limit in the two blanks analyzed with the test solution and in-life samples.

DETECTION LIMIT: The Bisphenol A method detection limit (MDL) was 500 µg/mL as determined by an MDL study. No data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed. In this analysis, sampling was performed by taking the sample material from flask through to analysis. Analyzing a spiked sample would be no different from analyzing a CCV.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSDs) for the two test solutions ranged from 0.859 to 3.29.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of Test Solution Concentrations Prepared and Analyzed on 11/20/2002

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	%RSD
80 mg/mL	WA2-14-W-F Rep1 R-1	81.2		
80 mg/mL	WA2-14-W-F Rep1 R-2	81.0	81.5	0.859
80 mg/mL	WA2-14-W-F Rep1 R-3	82.3		
120 mg/mL	WA2-14-X-F Rep1 R-1	125		
120 mg/mL	WA2-14-X-F Rep1 R-2	125	123	3.29
120 mg/mL	WA2-14-X-F Rep1 R-3	118		

Table 2. In-life and Post-Test Sample Concentrations

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
11/27/02	12/20/02	01/24/03	80 mg/mL	11-27 W-F R-1	83.4	104
11/27/02	12/20/02	01/24/03	120 mg/mL	11-27 X-F R-1	125	104
12/03/02	12/20/02	01/24/03	80 mg/mL	12-3 W-F R-1	81.4	102
12/03/02	12/20/02	01/24/03	120 mg/mL	12-3 X-F R-1	130	108
12/10/02	12/20/02	01/24/03	80 mg/mL	12-10 W-F R-1	87.5	109
12/10/02	12/20/02	01/24/03	120 mg/mL	12-10 X-F R-1	131	109
12/17/02	12/20/02	01/24/03	80 mg/mL	12-17 W-F R-1	78.9	99
12/17/02	12/20/02	01/24/03	120 mg/mL	12-17 X-F R-1	134	112
End of test	12/20/02	01/24/03	80 mg/mL	2-14 W-F Remain R2	80.1	100
End of test	12/20/02	01/24/03	120 mg/mL	2-14 X-F Remain R2	119	99

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
p,p'-DDE in Mazola Corn Oil

November 10, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved (One-over-one) By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory
1529 West Sequim Bay Road
Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology
Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
p,p'-DDE in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
p,p'-DDE in Mazola Corn Oil

Parameter	Chemical
Compound Name	p,p'-DDE
CAS #	72-55-9
Central File No.	CF-1832
Initial Receipt Date	10/25/2001
Expiration Date	10/2004
Manufacturer	Aldrich, Inc.
Lot Number	09020KU
Battelle Study #	WA 2-14-02-01
Method	SW 846, 8015B Modified

Executive Summary

The chemical purity of p,p'-DDE determined by the manufacturer was 99.4%. The purity result from Battelle-Sequim by GC-FID was determined to be 99.4%. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of DDE was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 6 weeks. Thus, stability testing of the DDE stock solution in corn oil was considered stable at both the 10 mg/mL and 20 mg/mL concentrations for the required testing period of 4.5 weeks.

Mazola corn oil (expiration dates 4-03 and 9-03) were purchased on 9-04-01 and 6-17-02 from local grocery stores, Mark and Pack and Quality Foods Center respectively, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 6-17-02 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn oil with an expiration date of 4-03 was 2.07 meq/kg (RSD = 5.9%). The average peroxide number in the Mazola corn oil with an expiration date of 9-03 was 1.38 meq/kg (RSD = 7.8%). This level of peroxide is consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 91% to 93%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA 2-14-02-01, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of DDE (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_DDE-cornoil.doc, PSTP_ WA-2-14_DDE-cornoil.doc, DSUM_ WA-2-10_2-14_2-23.xls, and DAF_WA-2-10_2-14_2-23.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, p,p'-DDE, (CAS No. 72-55-9, referred hereafter as DDE) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). The chemical was purchased from Aldrich, Inc. and lot number 09020KU was initially received on 10/25/2001 with an expiration date of 10/2004 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1832) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Corn oil (expiration dates 4-03 and 9-03) was purchased on 9-04-01 and 6-17-02 from local grocery stores, Mark and Pack and Quality Foods Center respectively, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 6-17-02 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-01

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: DDE (MSL CF 1832)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 10 mg/mL and 20 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Planned/proposed test duration: 4.5 weeks

Chemical Information

Chemical Name: DDE

CAS: 72-55-9

Any known purity information: may refer to attached documentation
Manufacturer's Purity Information: 99.4% pure
Any known stability information: may refer to attached documentation
Manufacturer's Stability Information: stable
Desired purity (%) for test? 95% or greater

Figure 1. EDSP Requisition Form for DDE

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	p,p'-DDE
CAS #	72-55-9
Central File No.	CF-1832
Initial Receipt Date	10/25/2001
Expiration Date	10/2004
Manufacturer	Aldrich, Inc.
Lot Number	09020KU
Manufacturer's Purity	99.4%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA 2-14-02-01
Method	SW 846, 8015B Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted by making a solution in hexane of about 100 µg/mL. This matrix was then run on a gas chromatograph with a flame ionization detector (GC-FID). A hexane blank was also run on the GC-FID. The purity was determined by first identifying the peaks in the chromatogram of the DDE that are the same as the peaks in the analysis of the blank hexane sample. The areas associated with these common peaks were then eliminated by inhibiting integration and the remaining peaks were reported as a percentage of the total peak area. The percentage associated with the largest peak represented the purity of DDE. The GC was set up with an auto sampler and a 30 m x 0.25 mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and the detector temperature at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. Stock solutions were prepared to arrive at the chemical concentrations requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

DDE stock matrices were prepared on 6-18-02 for testing as described in Table 2. Briefly, for the 10 mg/mL DDE stock, 0.5064 g was weighed into a 50 mL Class A volumetric flask and corn oil was added to the 50 mL mark. The solution was agitated by hand shaking for approximately five minutes until all of the DDE was dissolved. For the 20 mg/mL DDE stock, 1.0057 g was weighed into a 50 mL Class A volumetric flask and corn oil was added to the mark.

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA 2-14-02-01 12 Weeks	DDE	10 mg/mL	1832-1a-2	0.5064 g in 50 mL corn oil
		20 mg/mL	1832-1a-3	1.0057 g in 50 mL corn oil

The solution was agitated in a similar manner until all of the chemical was dissolved. All solutions were transferred to ashed, amber bottles. Bottles were labeled and stored at 4ºC ± 2ºC for the duration of the test.

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by chromatographic analysis. Triplicate aliquots of each concentration were tested. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

DDE stock solution was sampled by weighing ~1 g of sample into a 30 mL amber, ashed vial and adding 25 mL of hexane using a volumetric pipette. For samples 1832-1a-2 and 1832-1a-3, analysis was then conducted by adding 0.1 mL of the hexane solution and 0.02 mL of internal standard 5a androstane and 0.88 mL of hexane to the GC auto sampler vial. A corn oil blank was prepared the same way. This solution was then run on the GC-FID for quantification. The major peak determined during the purity analysis of DDE was used for this analysis. Continuing calibration verification (CCV) samples were analyzed to demonstrate on-going calibration accuracy.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fitted to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability are used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a GC-FID purity scan on the DDE. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for DDE and several very small peaks. The area of the DDE peak was 99.4% of the total area of all peaks in the chromatogram. Chemical purity of DDE determined by the manufacturer was 99.4% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 6-18-02. Chemical concentration was determined 11 times over a period of 12 weeks. The analytical and QC results are presented in Appendix C. A single preparation blank was analyzed with every batch for quality control purposes. There were no detectable concentrations of DDE in the blanks. CCV results ranged from 99.4% to 101%. Internal standards were analyzed with each sample and these results ranged from 93.4% to 111%. The MDL was 115 µg/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg as required for biological testing (Appendix C). The average peroxide number in the Mazola corn oil with an expiration date of 4-03 was 2.07 meq/kg (RSD = 5.9%). The average peroxide number in the Mazola corn oil with an expiration date of 9-03 was 1.38 meq/kg (RSD = 7.8%).

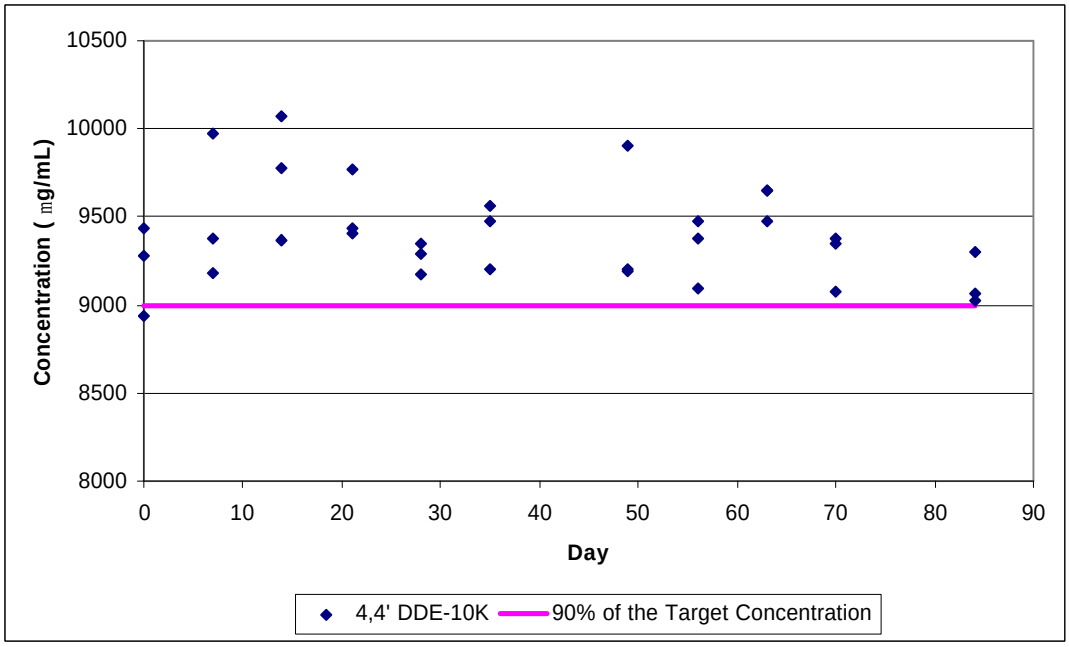
3.3 Statistical Results of Stability Trial

A plot of DDE with a target concentration of 10,000 µg/mL against time suggests very little chemical decay (Figure 2). Only one data point was less than 90% of the target concentration. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of DDE was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 11 weeks (Table 3). Thus, this stock solution was considered stable for the required 4.5-week testing period. The complete statistical analysis is presented in Appendix D.

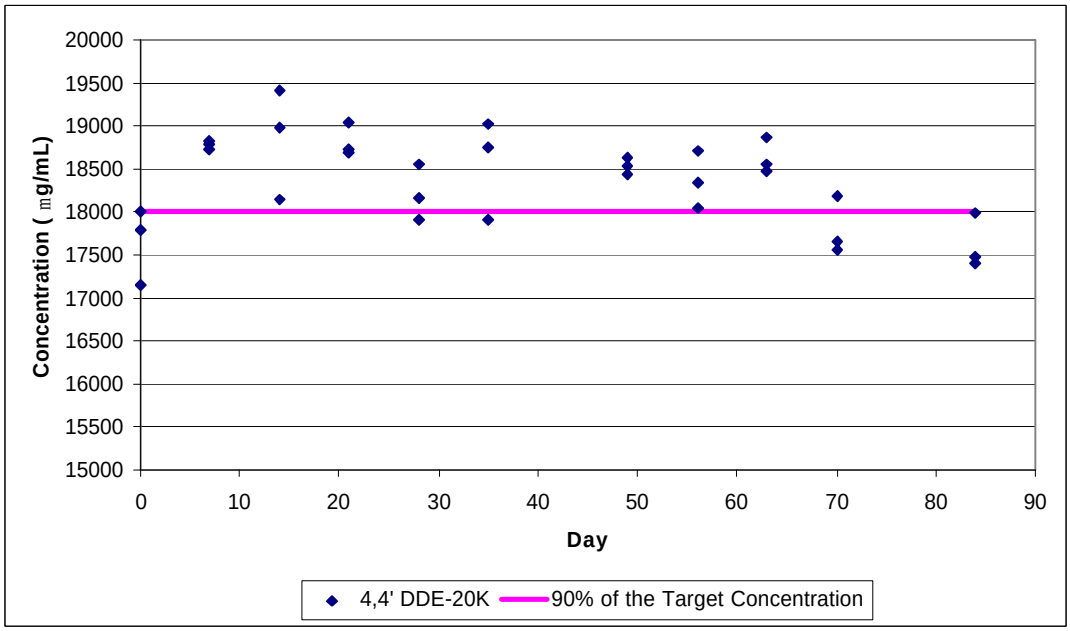
Eight observations of DDE with a target concentration of 20,000 µg/mL were less than 90% of the target concentration (Figure 2). Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of DDE was expected to stay greater than or equal to 90% of the target concentration for an estimated 6 weeks (Table 3). Thus, this stock solution was considered stable for the required testing period of 4.5 weeks. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses based on target concentrations ranged from 91% to 93%. The complete analysis is presented in Appendix E.



A



B

Figure 2. Observed Concentration of DDE with a Target Concentration of 10,000 mg/mL (A) and 20,000 mg/mL (B) Against Time

Table 3. Summary of Statistical Results for DDE

WA 2-14-02-01 Statistical Analysis conducted by Valerie Cullinan Using Minitab Version 13.32, Minitab Inc., 1999.	1832-1a-2 DDE-10K	1832-1a-3 DDE-20K
Target Concentration (μg/mL)	10000	20000
Number of determinations	1	1
Number of days tested	84	84
Number of replicates per day	3	3
Number of outliers removed	0	0
Number of observations removed	0	0
Overall Mean Concentration	9401	18349
95% Upper CL	9482.5	18509
error degrees of freedom	32	32
1-sample t-test of Ho: μ >= Target	S[a]	S
estimated intercept of ln(concentration) against time	9.1584	9.8300
estimated slope of ln(concentration) against time	-0.0003	-0.0003
standard error of slope	0.0002	0.0002
error degrees of freedom	31	31
Significance test of lack-of-fit for final model	NS[b]	S
Significance test of Ho: β = 0 vs. H1: β = 0	NS	NS
Lower 95% CL of β	-0.001	-0.001
Upper 95% CL of β	0.000	0.000
Maximum Percent Loss (using LCL)	0.5%	0.6%
Mean Percent Loss (using bhat)	0.2%	0.3%
LN(90% of Target)	9.1050	9.7981
Number of days until at 90% of Target (using LCL)	82	44
Conclusion using Target Concentration:	**Stable for 4.5 wks**	**Stable for 4.5 wks**

[a] Significant at α = 0.05
[b] Not significant at α = 0.05

4.0 CONCLUSIONS

Chemical purity of DDE determined by the manufacturer was 99.4%; purity determined by Battelle-Sequim was also 99.4%. Stability testing of DDE in corn oil concluded that the chemical was stable at both the 10 mg/mL and 20 mg/mL concentrations for a period of 4.5 weeks.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 91% to 93%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

ALDRICH

Certificate of Analysis

TEST	SPECIFICATION	LOT (09020KU) RESULTS
Product Name	4,4'-DDE	
Product Number	123897	
CAS Number	72559	
Formula	$C_{14}H_8Cl_4$	
Formula Weight	318.0	
APPEARANCE	WHITE CRYSTALS	WHITE CRYSTALS
INFRARED SPECTRUM	CONFORMS TO STRUCTURE AND STANDARD AS ILLUSTRATED ON PAGE 1026C OF EDITION I, VOLUME 1 OF 'THE ALDRICH LIBRARY OF FT-IR SPECTRA'.	CONFORMS TO STRUCTURE AND STANDARD AS ILLUSTRATED ON PAGE 1763B OF EDITION I, VOLUME 2 OF 'THE ALDRICH LIBRARY OF FT-IR SPECTRA'.
GAS LIQUID CHROMATOGRAPHY	98.5% (MINIMUM)	99.4 %
QUALITY CONTROL ACCEPTANCE DATE		AUGUST, 1999

David Swessel, Supervisor
Quality Control

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for DDE

Chemical Name: DDE (MSL CF Login 1832), CMS 173725

CAS Number: 72-55-9

Lot Number: 09020KU, stored at RT in Bldg5 Rm 219

Expiration date: 10/04

Manufacturer's Purity Information: 99.4%

Manufacturer's Stability Information: stable

MSL Purity Results:
Purity (%) To be determined at MSL by GC-FID scan

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: DDE

CAS: 72-55-9

Carrier(s): corn oil

Concentrations/Dilution Series: 10 and 20 mg/mL

Below MDL determined in Purity Analysis?

In vitro or in *vivo tests*? *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Planned/Proposed test duration: 4.5 weeks

Design of Stability Test: 10 and 20 mg/mL in glass at 4 deg. C in the dark for 12 weeks, analyzed weekly in triplicate by GC detector

Number of replicates: 3

Duration: 12 weeks, sampling each week

other factors:

Temperature regime(s): 4 deg. C

Test container type: Glass

Light or dark: Dark except when container is removed for sampling or handling

Other

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:

Manufacturer's certificate of analysis or purity

MSDS

Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
  - Chemical repository confirmatory test results of chemical identity and purity;
  - Chemical repository test results of lot-to-lot variation in chemical purity;
  - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. DDE concentration in Mazola Corn Oil (µg/mL)

Target Conc.	Sample ID	Date	DDE	Average	RSD	Recovery[1]
10000 ug/ml	1832-1a-2-1 R-1	6/18/2002	8940			
10000 ug/ml	1832-1a-2-1 R-2	6/18/2002	9277	9217	2.73%	92.2%
10000 ug/ml	1832-1a-2-1 R-3	6/18/2002	9434			
20000 ug/ml	1832-1a-3-1 R-1	6/18/2002	17796			
20000 ug/ml	1832-1a-3-1 R-2	6/18/2002	17144	17648	2.54%	88.2%
20000 ug/ml	1832-1a-3-1 R-3	6/18/2002	18004			
blank	Corn Oil (T=0)	6/19/2002	115 U			
10000 ug/ml	1832-1a-2-2 R-1	6/25/2002	9181			
10000 ug/ml	1832-1a-2-2 R-2	6/25/2002	9377	9511	4.36%	95.1%
10000 ug/ml	1832-1a-2-2 R-3	6/25/2002	9976			
20000 ug/ml	1832-1a-3-2 R-1	6/25/2002	18819			
20000 ug/ml	1832-1a-3-2 R-2	6/25/2002	18782	18776	0.24%	93.9%
20000 ug/ml	1832-1a-3-2 R-3	6/25/2002	18728			
blank	Corn Oil (week 1)	6/25/2002	115 U			
10000 ug/ml	1832-1a-2-3 R-1	7/2/2002	9368			
10000 ug/ml	1832-1a-2-3 R-2	7/2/2002	9773	9738	3.64%	97.4%
10000 ug/ml	1832-1a-2-3 R-3	7/2/2002	10074			
20000 ug/ml	1832-1a-3-3 R-1	7/2/2002	18140			
20000 ug/ml	1832-1a-3-3 R-2	7/2/2002	19420	18850	3.45%	94.3%
20000 ug/ml	1832-1a-3-3 R-3	7/2/2002	18991			
blank	Corn Oil (week 2)	7/2/2002	115 U			
10000 ug/ml	1832-1a-2-4 R-1	7/9/2002	9771			
10000 ug/ml	1832-1a-2-4 R-2	7/9/2002	9435	9537	2.13%	95.4%
10000 ug/ml	1832-1a-2-4 R-3	7/9/2002	9403			
20000 ug/ml	1832-1a-3-4 R-1	7/9/2002	18694			
20000 ug/ml	1832-1a-3-4 R-2	7/9/2002	18736	18821	0.98%	94.1%
20000 ug/ml	1832-1a-3-4 R-3	7/9/2002	19034			
blank	Corn Oil (week 3)	7/9/2002	115 U			
10000 ug/ml	1832-1a-2-5 R-1	7/16/2002	9172			
10000 ug/ml	1832-1a-2-5 R-2	7/16/2002	9351	9270	0.98%	92.7%
10000 ug/ml	1832-1a-2-5 R-3	7/16/2002	9286			
20000 ug/ml	1832-1a-3-5 R-1	7/16/2002	18169			
20000 ug/ml	1832-1a-3-5 R-2	7/16/2002	18553	18210	1.78%	91.1%
20000 ug/ml	1832-1a-3-5 R-3	7/16/2002	17908			
blank	Corn Oil (week 4)	7/16/2002	115 U			
10000 ug/ml	1832-1a-2-6 R-1	7/23/2002	9199			
10000 ug/ml	1832-1a-2-6 R-2	7/23/2002	9472	9410	1.99%	94.1%
10000 ug/ml	1832-1a-2-6 R-3	7/23/2002	9559			
20000 ug/ml	1832-1a-3-6 R-1	7/23/2002	19017			
20000 ug/ml	1832-1a-3-6 R-2	7/23/2002	17911	18563	3.12%	92.8%
20000 ug/ml	1832-1a-3-6 R-3	7/23/2002	18759			
blank	Corn Oil (week 5)	7/23/2002	115 U			
10000 ug/ml	1832-1a-2-7 R-1	8/6/2002	9192			
10000 ug/ml	1832-1a-2-7 R-2	8/6/2002	9206	9435	4.33%	94.4%
10000 ug/ml	1832-1a-2-7 R-3	8/6/2002	9907			
20000 ug/ml	1832-1a-3-7 R-1	8/6/2002	18542			
20000 ug/ml	1832-1a-3-7 R-2	8/6/2002	18437	18541	0.55%	92.7%
20000 ug/ml	1832-1a-3-7 R-3	8/6/2002	18643			
blank	Corn Oil (week 7)	8/6/2002	115 U			

TABLE C.1, Continued

Target Conc.	Sample ID	Date	DDE	Average	RSD	Recovery[1]
10000 ug/ml	1832-1a-2-8 R-1	8/13/2002	9097			
10000 ug/ml	1832-1a-2-8 R-2	8/13/2002	9374	9316	2.10%	93.2%
10000 ug/ml	1832-1a-2-8 R-3	8/13/2002	9476			
20000 ug/ml	1832-1a-3-8 R-1	8/13/2002	18053			
20000 ug/ml	1832-1a-3-8 R-2	8/13/2002	18331	18363	1.78%	91.8%
20000 ug/ml	1832-1a-3-8 R-3	8/13/2002	18706			
blank	Corn Oil (week 8)	8/13/2002	115 U			
10000 ug/ml	1832-1a-2-9 R-1	8/20/2002	9472			
10000 ug/ml	1832-1a-2-9 R-2	8/20/2002	9652	9590	1.06%	95.9%
10000 ug/ml	1832-1a-2-9 R-3	8/20/2002	9646			
20000 ug/ml	1832-1a-3-9 R-1	8/20/2002	18476			
20000 ug/ml	1832-1a-3-9 R-2	8/20/2002	18875	18638	1.13%	93.2%
20000 ug/ml	1832-1a-3-9 R-3	8/20/2002	18563			
blank	Corn Oil (week 9)	8/20/2002	115 U			
10000 ug/ml	1832-1a-2-10 R-1	8/27/2002	9071			
10000 ug/ml	1832-1a-2-10 R-2	8/27/2002	9379	9264	1.82%	92.6%
10000 ug/ml	1832-1a-2-10 R-3	8/27/2002	9343			
20000 ug/ml	1832-1a-3-10 R-1	8/27/2002	17659			
20000 ug/ml	1832-1a-3-10 R-2	8/27/2002	17562	17802	1.88%	89.0%
20000 ug/ml	1832-1a-3-10 R-3	8/27/2002	18184			
blank	Corn Oil (week 10)	8/27/2002	115 U			
10000 ug/ml	1832-1a-2-12 R-1	9/10/2002	9025			
10000 ug/ml	1832-1a-2-12 R-2	9/10/2002	9060	9127	1.61%	91.3%
10000 ug/ml	1832-1a-2-12 R-3	9/10/2002	9295			
20000 ug/ml	1832-1a-3-12 R-1	9/10/2002	17398			
20000 ug/ml	1832-1a-3-12 R-2	9/10/2002	17478	17625	1.85%	88.1%
20000 ug/ml	1832-1a-3-12 R-3	9/10/2002	17998			
blank	Corn Oil (week 12)	9/10/2002	115 U			

[1] Recovery is relative to the target concentration
U = Not detected at a value greater than the MDL

Table C.2. CCV Data for DDE Concentration in Mazola Corn Oil

Time	Sample Name	DDE (µg/mL)	Recovery	PD
T=0	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
Week 1	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
Week 2	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.60%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
Week 3	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
Week 4	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
Week 5	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.60%
Week 7	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
Week 8	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
Week 9	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
Week 10	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
Week 12	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%

Text Box C1. Calibration Standard Preparation

Calibration Standard EDSP Mix 1
Calibrations were performed using a five-point calibration curve labeled EDSP Mix 1 A thru E. This mix is used for Atrazine, Fenarimol, p,p'-DDE, Methoxychlor and Vinclozolin analyzed by GC-FID. These standards were made by serial dilutions of standards for each compound. • Atrazine standard was made by weighing 0.0499 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with Methylene chloride and labeled 1826-1-1. • Fenarimol standard was made by weighing 0.0506 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1829B-1. • p,p'-DDE standard was made by weighing 0.0501 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1832-1a-1. • Methoxychlor standard was made by weighing 0.0513 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1808-1-3. • Vinclozolin standard was made by weighing 0.0512 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1779-78. This analysis used an internal standard, in this case 5a androstane, which is made by weighing 0.0511 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane, this is then labeled REP7. The EDSP Mix 1 series (A through E) was made as follows. • Solution A, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 0.02 ml REP7 added to a 10 ml volumetric flask and diluted to the mark with hexane. • Solution B, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution C, 0.25 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution D, 0.1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane. • Solution E, 0.05 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane.

Table C.3. Internal Standards Data for DDE in Mazola Corn Oil

Sample Name	Date	5A Androstane Recovery
1832-1a-2-1 R-1	6/18/2002	108%
1832-1a-2-1 R-2	6/18/2002	107%
1832-1a-2-1 R-3	6/18/2002	107%
1832-1a-3-1 R-1	6/18/2002	107%
1832-1a-3-1 R-2	6/18/2002	108%
1832-1a-3-1 R-3	6/18/2002	105%
1832-1a-2-2 R-1	6/25/2002	104%
1832-1a-2-2 R-2	6/25/2002	103%
1832-1a-2-2 R-3	6/25/2002	102%
1832-1a-3-2 R-1	6/25/2002	103%
1832-1a-3-2 R-2	6/25/2002	105%
1832-1a-3-2 R-3	6/25/2002	105%
1832-1a-2-3 R-1	7/2/2002	102%
1832-1a-2-3 R-2	7/2/2002	101%
1832-1a-2-3 R-3	7/2/2002	97.3%
1832-1a-3-3 R-1	7/2/2002	104%
1832-1a-3-3 R-2	7/2/2002	98.1%
1832-1a-3-3 R-3	7/2/2002	101%
1832-1a-2-4 R-1	7/9/2002	96.3%
1832-1a-2-4 R-2	7/9/2002	99.7%
1832-1a-2-4 R-3	7/9/2002	101%
1832-1a-3-4 R-1	7/9/2002	101%
1832-1a-3-4 R-2	7/9/2002	99.6%
1832-1a-3-4 R-3	7/9/2002	98.0%
1832-1a-2-5 R-1	7/16/2002	103%
1832-1a-2-5 R-2	7/16/2002	104%
1832-1a-2-5 R-3	7/16/2002	105%
1832-1a-3-5 R-1	7/16/2002	107%
1832-1a-3-5 R-2	7/16/2002	105%
1832-1a-3-5 R-3	7/16/2002	108%
1832-1a-2-6 R-1	7/23/2002	103%
1832-1a-2-6 R-2	7/23/2002	103%
1832-1a-2-6 R-3	7/23/2002	102%
1832-1a-3-6 R-1	7/23/2002	104%
1832-1a-3-6 R-2	7/23/2002	107%
1832-1a-3-6 R-3	7/23/2002	103%
1832-1a-2-7 R-1	8/6/2002	103%
1832-1a-2-7 R-2	8/6/2002	104%
1832-1a-2-7 R-3	8/6/2002	104%
1832-1a-3-7 R-1	8/6/2002	102%
1832-1a-3-7 R-2	8/6/2002	103%
1832-1a-3-7 R-3	8/6/2002	93.4%
1832-1a-2-8 R-1	8/13/2002	102%
1832-1a-2-8 R-2	8/13/2002	104%
1832-1a-2-8 R-3	8/13/2002	105%
1832-1a-3-8 R-1	8/13/2002	108%
1832-1a-3-8 R-2	8/13/2002	105%
1832-1a-3-8 R-3	8/13/2002	104%

Table C3. continued

Sample Name	Date	5A Androstane Recovery
1832-1a-2-9 R-1	8/20/2002	103%
1832-1a-2-9 R-2	8/20/2002	103%
1832-1a-2-9 R-3	8/20/2002	103%
1832-1a-3-9 R-1	8/20/2002	106%
1832-1a-3-9 R-2	8/20/2002	106%
1832-1a-3-9 R-3	8/20/2002	106%
1832-1a-2-10 R-1	8/27/2002	111%
1832-1a-2-10 R-2	8/27/2002	109%
1832-1a-2-10 R-3	8/27/2002	109%
1832-1a-3-10 R-1	8/27/2002	111%
1832-1a-3-10 R-2	8/27/2002	111%
1832-1a-3-10 R-3	8/27/2002	109%
1832-1a-2-12 R-1	9/10/2002	104%
1832-1a-2-12 R-2	9/10/2002	104%
1832-1a-2-12 R-3	9/10/2002	103%
1832-1a-3-12 R-1	9/10/2002	104%
1832-1a-3-12 R-2	9/10/2002	105%
1832-1a-3-12 R-3	9/10/2002	103%

Table C.4. Peroxide concentration in Mazola Corn Oil (meq/kg) measured on 6/17/02

Sample	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	0.75	0.005	5.00	0.75		
Mazola Corn Oil Expiration 9-03 R-1	1.6	0.005	5.43	1.47		
Mazola Corn Oil Expiration 9-03 R-2	1.5	0.005	5.32	1.41	1.38	7.8%
Mazola Corn Oil Expiration 9-03 R-3	1.2	0.005	4.75	1.26		
Mazola Corn Oil Expiration 4-03 R-1	2.0	0.005	5.18	1.93		
Mazola Corn Oil Expiration 4-03 R-2	2.2	0.005	5.09	2.16	2.07	5.9%
Mazola Corn Oil Expiration 4-03 R-3	2.5	0.005	5.21	2.11		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-01
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

11/25/2002 11:22:30 AM

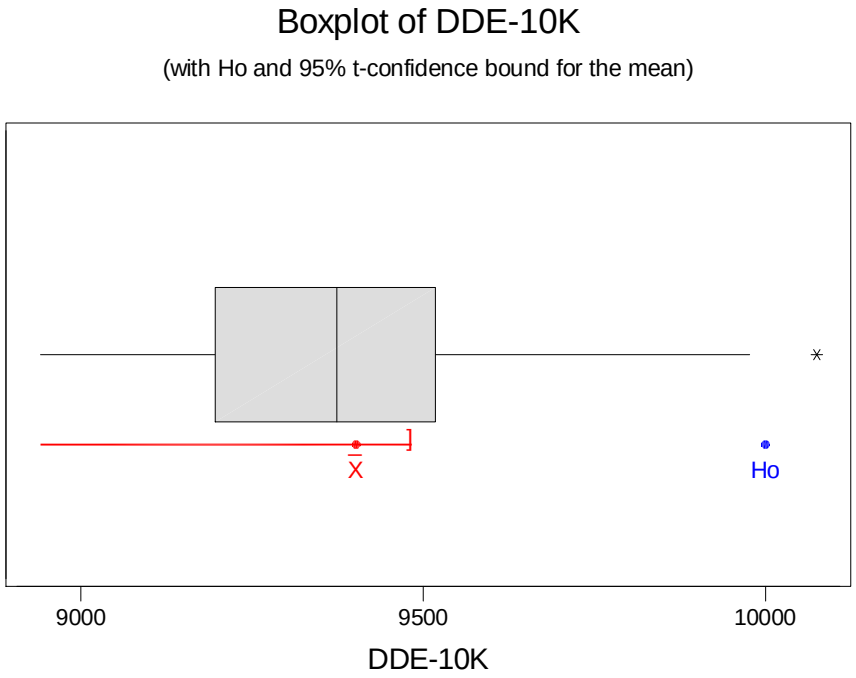
Analysis of DDE-10k in corn oil

- Test to determine if the data are from a population with mean of 10000.

One-Sample T: DDE-10K

```
Test of mu = 10000 vs mu < 10000

Variable          N      Mean     StDev   SE Mean
DDE-10K          33    9401.3     275.3      47.9

Variable      95.0% Upper Bound        T      P
DDE-10K                  9482.5   -12.49  0.000
```

t Boxplot of DDE-10K



- Nonparametric Test for outlier.

```
Outliers are < Median-3*IQD OR > Median+3*IQD
Boundary for outliers are values <    8409.27  and >    10338.3
No outliers
```

- Transform data to natural logarithm and conduct regression analysis.

Week	Rep	Ln(Concentration)
0	1	9.0983
0	2	9.1353
0	3	9.1520
7	1	9.1249
7	2	9.1460
7	3	9.2080
14	1	9.1450
14	2	9.1874
14	3	9.2177
21	1	9.1872
21	2	9.1522
21	3	9.1488
28	1	9.1239
28	2	9.1433
28	3	9.1363
35	1	9.1269
35	2	9.1561
35	3	9.1652
49	1	9.1261
49	2	9.1276
49	3	9.2010
56	1	9.1157
56	2	9.1457
56	3	9.1565
63	1	9.1561
63	2	9.1749
63	3	9.1743
70	1	9.1128
70	2	9.1462
70	3	9.1424
84	1	9.1077
84	2	9.1116
84	3	9.1373

  - Conducts Simple Linear Regression

Regression Analysis: DDE-10K versus Day

The regression equation is
DDE-10K = 9.16 -0.000263 Day

Predictor	Coef	SE Coef	T	P
Constant	9.15840	0.00889	1030.19	0.000
Day	-0.0002628	0.0001897	-1.39	0.176

S = 0.02861 R-Sq = 5.8% R-Sq(adj) = 2.8%

Analysis of Variance

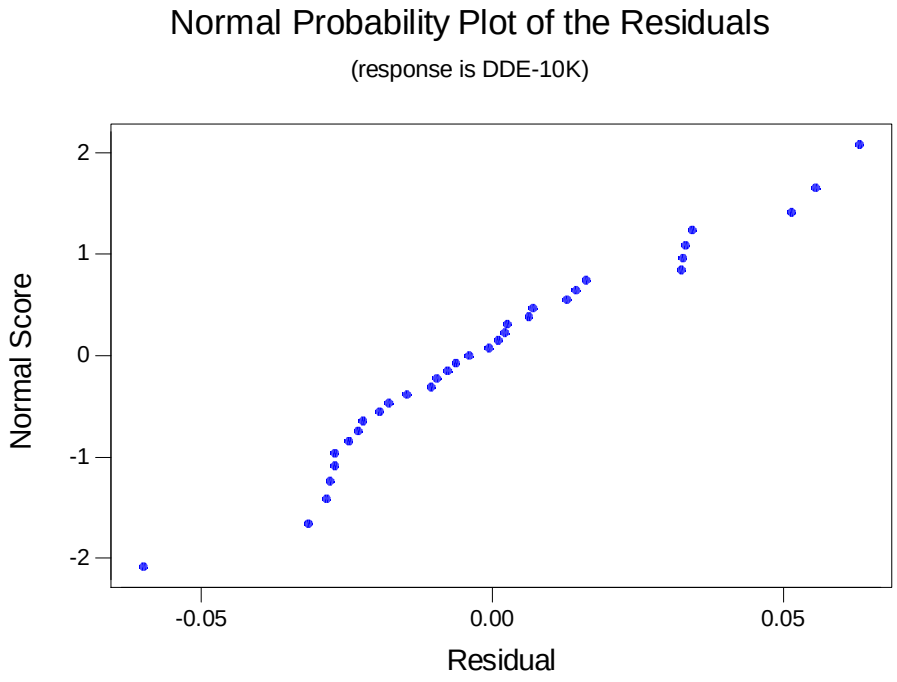
Source	DF	SS	MS	F	P
Regression	1	0.0015703	0.0015703	1.92	0.176
Residual Error	31	0.0253747	0.0008185		
Lack of Fit	9	0.0095986	0.0010665	1.49	0.214
Pure Error	22	0.0157761	0.0007171		
Total	32	0.0269450			

Unusual Observations

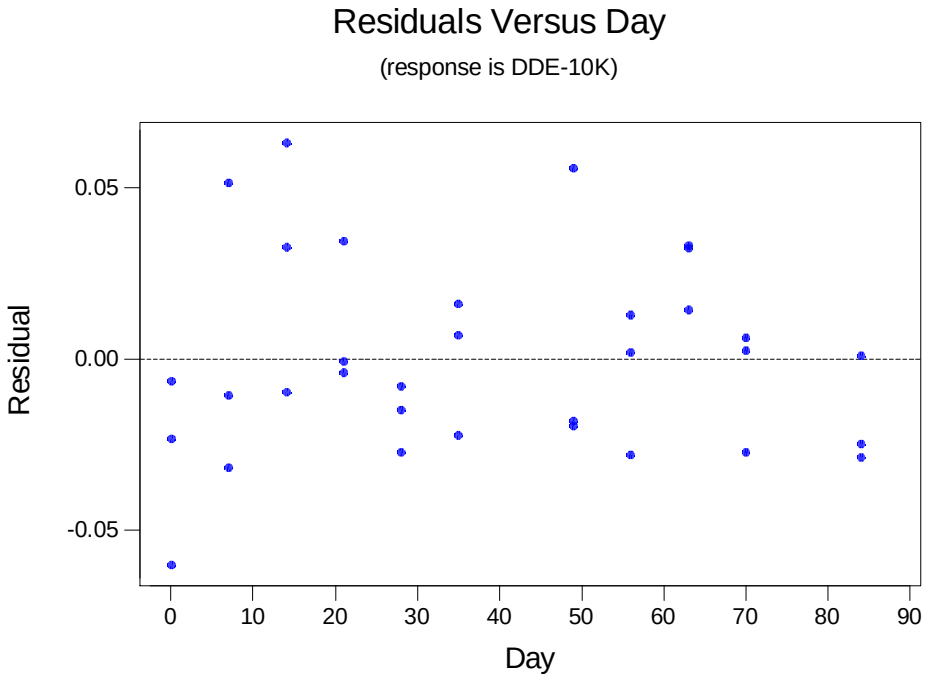
Obs	Day	DDE-10K	Fit	SE Fit	Residual	St Resid
1	0.0	9.09834	9.15840	0.00889	-0.06006	-2.21R
9	14.0	9.21775	9.15472	0.00685	0.06303	2.27R

R denotes an observation with a large standardized residual

Normplot of Residuals for DDE-10K



Residuals from DDE-10K vs Day



- Power analysis for t-test of slope less than zero

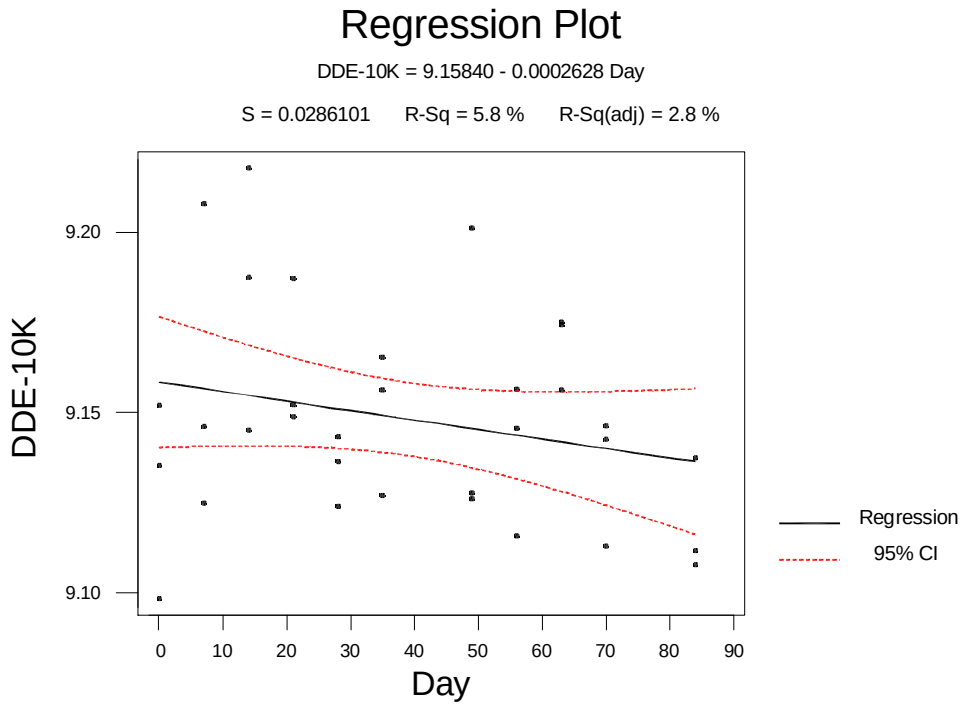
Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0286101

Sample
  Size   Power  Difference
    31  0.9900     -0.0209
```

- That means we would detect a mean of 9.1894 as significantly less than ln(10000) = 9.2103 or a change of 9793 from 10000 = 2.1% loss.

- Fit 95% confidence bands about the fitted simple linear model

Fitted Line Plot: DDE-10K versus Day



Conclusion – stable for 4.5 weeks.

WA-2-14-02-01
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

11/25/2002 11:22:30 AM

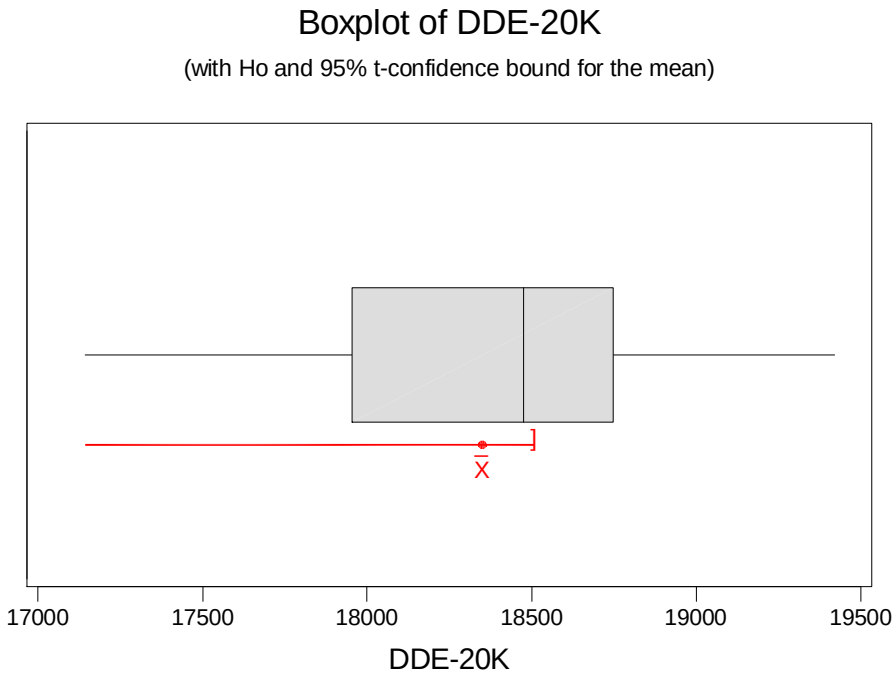
Analysis of DDE-20k in corn oil

- Test to determine if the data are from a population with mean of 20000.

One-Sample T: DDE-20K

```
Test of mu = 20000 vs mu < 20000

Variable          N      Mean     StDev   SE Mean
DDE-20K          33   18348.9     543.0      94.5

Variable      95.0% Upper Bound        T      P
DDE-20K                 18509.0   -17.47  0.000
```

t Boxplot of DDE-20K



- Nonparametric Test for outlier.

```
Outliers are < Median-3*IQD OR > Median+3*IQD
Boundary for outliers are values <    16096.0  and >    20856.5
No outliers
```

- Transform data to natural logarithm and conduct regression analysis.

Week	Rep	Ln(Concentration)
0	1	9.7868
0	2	9.7494
0	3	9.7984
7	1	9.8426
7	2	9.8406
7	3	9.8378
14	1	9.8059
14	2	9.8741
14	3	9.8517
21	1	9.8360
21	2	9.8382
21	3	9.8540
28	1	9.8075
28	2	9.8284
28	3	9.7930
35	1	9.8531
35	2	9.7932
35	3	9.8394
49	1	9.8278
49	2	9.8221
49	3	9.8332
56	1	9.8011
56	2	9.8164
56	3	9.8366
63	1	9.8242
63	2	9.8456
63	3	9.8290
70	1	9.7790
70	2	9.7735
70	3	9.8083
84	1	9.7641
84	2	9.7687
84	3	9.7980

  - Conducts Simple Linear Regression

Regression Analysis: DDE-20K versus Day

The regression equation is
DDE-20K = 9.83 -0.000338 Day

Predictor	Coef	SE Coef	T	P
Constant	9.83000	0.00896	1097.18	0.000
Day	-0.0003377	0.0001912	-1.77	0.087

S = 0.02883 R-Sq = 9.1% R-Sq(adj) = 6.2%

Analysis of Variance

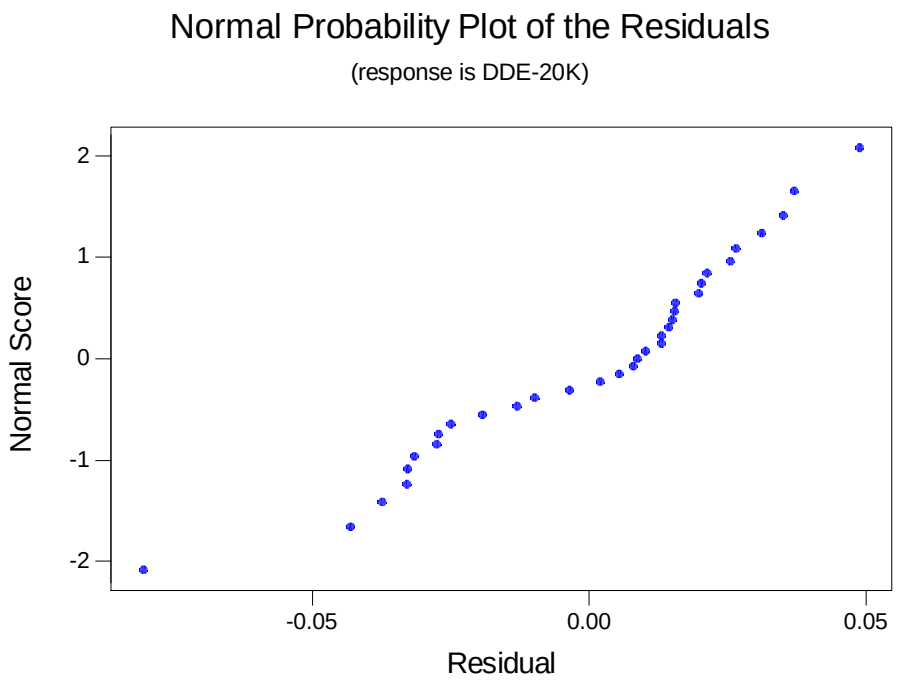
Source	DF	SS	MS	F	P
Regression	1	0.0025931	0.0025931	3.12	0.087
Residual Error	31	0.0257720	0.0008314		
Lack of Fit	9	0.0169143	0.0018794	4.67	0.002
Pure Error	22	0.0088577	0.0004026		
Total	32	0.0283651			

Unusual Observations

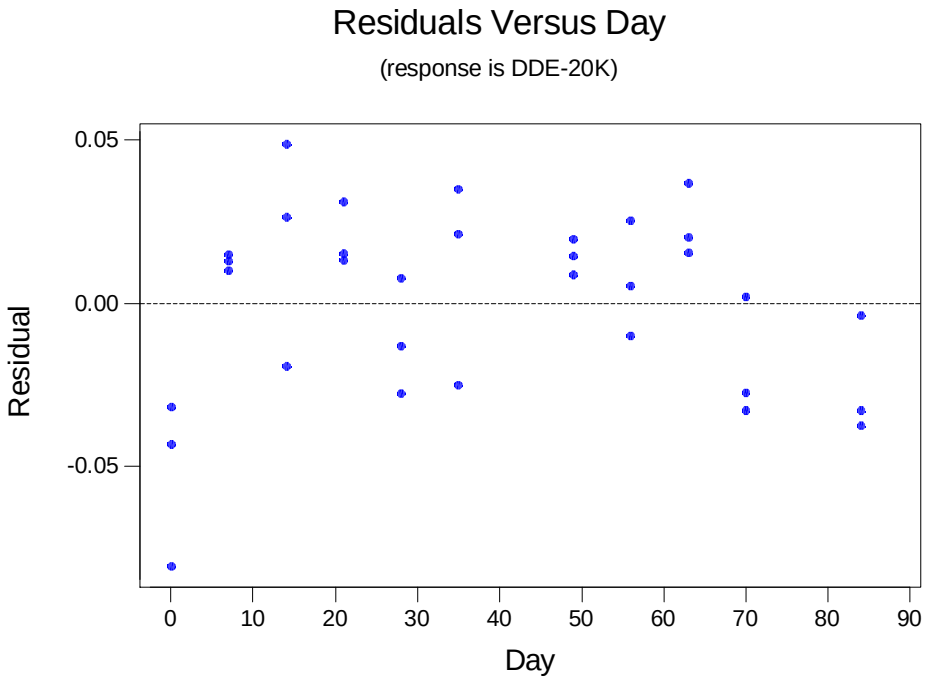
Obs	Day	DDE-20K	Fit	SE Fit	Residual	St Resid
2	0.0	9.74938	9.83000	0.00896	-0.08062	-2.94R

R denotes an observation with a large standardized residual

Normplot of Residuals for DDE-20K



Residuals from DDE-20K vs Day



- Power analysis for t-test of slope less than zero

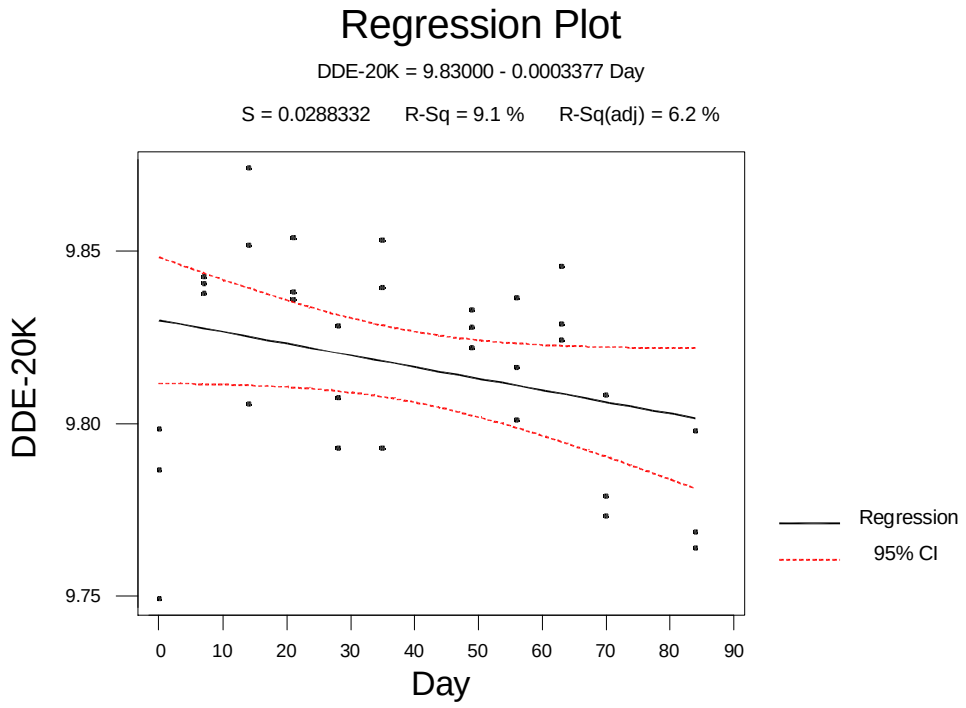
Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0288332

Sample
  Size   Power  Difference
    31  0.9900     -0.0211
```

- That means we would detect a mean of 9.8824 as significantly less than ln(20000) = 9.9035 or a change of 19582 from 20000 = 2.1% loss.

- Fit 95% confidence bands about the fitted simple linear model

Fitted Line Plot: DDE-20K versus Day



Conclusion – stable for 4.5 weeks.

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: p,p'-DDE in-life test solution samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: p,p'-DDE in corn oil

TEST SOLUTION SAMPLE CUSTODY AND PROCESSING:

Test solution samples were prepared by the EDSP Chemical Repository, Sequim, WA, using p,p'-DDE (CAS 72-55-9, CF 1832, Aldrich # 09020KU, expiration date 10/04) dissolved in Mazola corn oil (corn oil was from containers with the following expiration dates: 6/12/03, 1/1/04, and 4/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time. Samples were prepared at two test concentrations for all replicates in the male-only exposure; 10 mg/mL and 20 mg/mL. The 10 mg/mL concentration was prepared by dissolving 2.0 g of p,p'-DDE in 184 g of corn oil in a pre-cleaned amber glass container. The 20 mg/mL concentration was prepared by dissolving 4.0 g of p,p'-DDE in 182 g of corn oil.

Samples for male rat exposures were prepared at three different times:
Replicate 1 – prepared on 09/09/02 and shipped on 09/26/02
Replicate 2 – prepared on 10/02/02 and shipped on 10/03/02
Replicate 3 – prepared on 11/03/02 and shipped 11/04/02.

Note: Only samples prepared on 09/09/02 were analyzed to verify concentrations of p,p'-DDE. These values are reported in Table 1.

The test solution was sampled four times during the male test (10/07/02, 10/14/02, 10/21/02, and 10/28/02). Data for the in-life samples are reported in Table 2 for male exposures. Table 3 provides results of analysis of remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test.

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:

The container was placed on a magnetic stir plate and stirred. 1 mL triplicate samples were removed and each placed in a tared 60 mL amber-glass bottle. The weight of the sample was determined gravimetrically. A 1 g subsample was removed, placed in a 30 mL amber glass ashed vial, and 25 mL of hexane (JT Baker lot number X40E12) was added and the bottle agitated to mix. Then, 0.1 mL sample and 0.02 mL internal standard, 5a androstane, and 0.88 mL hexane were transferred to an auto sampler vial.

In-life and Returned Container Samples:

In-life and returned containers were analyzed the same way. Some of the returned containers were returned empty, so only containers with sufficient material were analyzed.

The samples were removed from the refrigerator and allowed to warm to room temperature. About 1 mL was sampled and placed in a tared 30 mL amber glass bottle. The weight of the sample was determined gravimetrically. 25 mL of hexane was added and the bottle agitated to mix. Then 0.1 mL was transferred to a 1.8 mL vial with 0.02 mL of internal standard solution containing 5a androstane, and 0.88 mL hexane.

SAMPLE ANALYSIS

The samples were analyzed by gas chromatograph (GC) with a flame ionization detector (FID). The GC was set up with an auto sampler and a 30-m x 0.25-mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and the detector temperature at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution.

Data Quality Objectives:	**Control Limits**
Procedural Blank	<5 X MDL
Blank Spike Recovery	40% - 120%
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: GC-FID

CALIBRATION: Calibration using a five-point curve was done using standards EDSP Mix 1 (see Appendix C) with a continuing calibration verification (CCV) sample analyzed every 10 samples.

CONTINUING STANDARD RECOVERY: Percent recovery results for initial and CCV samples analyzed with the in-life sample data set ranged from 91% to 117% with a mean recovery of 100%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK p,p'-DDE was not detected above the detection limit in the corn-oil blank analyzed with the test solution and in-life samples.

DETECTION LIMIT: The p,p'-DDE method detection limit (MDL) in corn oil was 115 ug/mL as determined by an MDL study. No data below this value were reported.

BLANK SPIKE SAMPLES Blank spike samples were not analyzed. In this analysis, sampling was performed by taking the sample material from flask through to analysis. Analyzing a spiked sample would be no different from analyzing a CCV.

INTERNAL STANDARD 5a androstane was spiked into each sample and analyzed as the internal standard. Average percent recovery results ranged from 99% to 103%. There were no cases in which the percent recovery of the internal standard exceeded the acceptance range of 40% to 120%.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSD) for the two test solutions ranged from 1.34 to 2.34.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of p,p'-DDE Test Solution Concentrations for Male Exposures

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	% RSD
R-1; 9/9/02				
10 mg/mL	2-14 –N-M R-1, R-1	9.42		
10 mg/mL	2-14 –N-M R-1, R-2	9.14	9.19	2.34
10 mg/mL	2-14 –N-M R-1, R-3	9.00		
20 mg/mL	2-14 –P-M R-1, R-1	18.4		
20 mg/mL	2-14 –P-M R-1, R-2	18.3	18.2	1.34
20 mg/mL	2-14 –P-M R-1, R-3	18.0		

Table 2. p,p'-DDE In-life Sample - Males

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
10/07/02	11/13/02	11/23/02	10 mg/mL	WA2-14N-M 10-7 Vial	9.30	93%
10/14/02	11/13/02	11/23/02	10 mg/mL	WA2-14N-M 10-14Vial	9.29	93%
10/21/02	11/13/02	11/23/02	10 mg/mL	WA2-14N-M 10-21Vial	9.34	93%
10/28/02	11/13/02	11/23/02	10 mg/mL	WA2-14N-M 10-28Vial	9.30	93%
10/07/02	11/13/02	11/23/02	20 mg/mL	WA2-14P-M 10-7 Vial	18.1	91%
10/14/02	11/13/02	11/23/02	20 mg/mL	WA2-14P-M 10-14Vial	18.2	91%
10/21/02	11/13/02	11/23/02	20 mg/mL	WA2-14P-M 10-21Vial	18.4	92%
10/28/02	11/13/02	11/23/02	20 mg/mL	WA2-14P-M 10-28Vial	–[(a)]	–

(a) – Missing sample; not on list of returned samples

Table 3. Post-Test p,p'-DDE Sample Concentrations for Formulations Returned to Battelle from RTI

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
Male Exposures						
11/03/02	11/13/02	11/22/02	10 mg/mL	WA 2-14-N-M Rep3Jar	9.40	94%
11/03/02	11/13/02	11/22/02	20 mg/mL	WA 2-14-P-M Rep3Jar	20.4	102%

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-004: Atrazine, DDE, vinclozolin, Methoxychlor, Fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[X]	Protocol
[ ]	SOP	[ ]	Method	[ ]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: 2.3 of protocol WA 2-14 states "an aliquot of each level per formulation will be analyzed"

DEVIATION: Each dose level was tested in the first preparation for each chemical. However, subsequent batches were not always analyzed.

REASON/IMPACT: No impact. Subsequent batches were prepared using the same methods and procedures as the first batches.
PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action required.

ACTIONS TO PREVENT RECURRENCE: Upper management will review the analyses schedule prior to the start of the studies.

Approval:

Michael Blanton,
WAL — Date 11-3-03

Eric Crecelius,
Study Director
Chemical Repository — Date 11-3-03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Fenarimol in Mazola Corn Oil

November 10, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory
1529 West Sequim Bay Road
Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology
Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Fenarimol in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Fenarimol in Mazola Corn Oil

Parameter	Chemical
Compound Name	Fenarimol
CAS #	60168-88-9
Central File No.	CF-1829
Initial Receipt Date	9/6/2002
Expiration Date	06/07
Manufacturer	ChemService, Inc.
Lot Number	287-5B
Battelle Study #	WA 2-14-02-02
Method	SW 846, 8015B Modified

Executive Summary

The chemical purity of fenarimol determined by the manufacturer was 99.5%. The purity result from Battelle-Sequim by GC-FID was determined to be 99.7%. Two concentrations of fenarimol were tested for stability with target concentrations of 10 mg/mL and 50 mg/mL. Based on the final regression model and the lower 95% confidence limit of the slope, the 10 mg/mL concentration of fenarimol was expected to stay greater than or equal to 90% of the target concentration for an unlimited time. However, based on the final regression model and the lower 95% confidence limit of the slope, the 50 mg/mL concentration of fenarimol was expected to stay greater than or equal to 90% of the target concentration for only 6 weeks. Thus, the stability of fenarimol was concluded to be stable for only 6 weeks of the required testing and holding time of 12 weeks.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries based on target concentrations for all doses ranged from 99.8% to 116%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA 2-14-02-02, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of fenarimol (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_Fenarimol-cornoil.doc, PSTP_WA-2-14_Fenarimol-cornoil.doc, DSUM_WA2-14_Atrazine-Fenarimol-crnoil.xls, and DAF_WA 2 14_Atrazine-Fenerimol-crnoil.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, fenarimol, (CAS No. 60168-88-9) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Fenarimol was purchased from ChemService, Inc. and lot number 287-5B was initially received on 9/6/2002 with an expiration date of 06/07 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1829) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Mazola corn oil with expiration dates of 6/03 and 1/04 were purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-02

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Fenarimol (MSL CF 1829)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 10 mg/mL and 50 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Planned/proposed testing/holding duration: 12 weeks

Chemical Information

Chemical Name: Fenarimol

CAS: 60168-88-9

Any known purity information: may refer to attached documentation

Manufacturer's Purity Information: 99.5% pure

Any known stability information: may refer to attached documentation

Manufacturer's Stability Information: stable

Desired purity (%) for test? 95% or greater

Figure 1. EDSP Requisition Form for Fenarimol

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Fenarimol
CAS #	60168-88-9
Central File No.	CF-1829
Initial Receipt Date	9/6/2002
Expiration Date	06/07
Manufacturer	ChemService, Inc.
Lot Number	287-5B
Manufacturer's Purity	99.5%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA 2-14-02-02
Method	SW 846, 8015B Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted by making a solution in hexane of about 100 µg/mL. This matrix was then run on a gas chromatograph with a flame ionization detector (GC-FID). A hexane blank was also run on the GC-FID. The purity was determined by first identifying the peaks in the chromatogram of the fenarimol that were the same as the peaks in the analysis of the blank hexane sample. The areas associated with these common peaks were then eliminated by inhibiting integration and the remaining peaks were reported as a percentage of the total peak area. The percentage associated with the largest peak represented the purity of fenarimol. The GC was set up with an auto sampler and a 30 m x 0.25 mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270 ºC and the detector temperature at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. Stock solutions were prepared at the chemical concentrations requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

Fenarimol stock matrices were prepared on 08/22/02 for testing as described in Table 2. Briefly, for the 10 mg/mL fenarimol, 2.0 g were weighed into a 250 mL amber wide-mouth jar containing 180 g corn oil, a stir bar was added, and the solution was mixed on a stir plate to suspend the mixture. For the 50 mg/mL fenarimol concentration, 9.5 g were weighed into a 250 mL amber glass wide-mouth jar containing 168 g corn oil and handled as described above.

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA 2-14-02-02 12 weeks	Fenarimol	10 mg/mL	1829-1-2	2.0 g in 180 g Mazola corn oil
		50 mg/mL	1829-1-3	9.5 g in 168 g Mazola corn oil

All solutions were transferred to ashed, amber glass bottles. Bottles were labeled and stored at 4ºC ± 2ºC for the duration of the test.

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentrations were determined by chromatographic analysis. Triplicate aliquots of the stock solutions were tested. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

A Fenarimol stock solution was sampled by weighing ~1 g of sample into a 30 mL amber glass, ashed vial and adding 25 mL of methylene chloride using a volumetric pipette. For samples 1829-1-2 analysis was then conducted by adding 0.1 mL of the methylene chloride solution and 0.02 mL of internal standard 5a androstane and 0.88 mL of hexane to the GC auto sampler vial. For samples 1829-1-3, 0.025 mL of the methylene chloride solution was added to a GC auto sampler vial with 0.02 mL of internal standard 5a androstane and 0.955 mL hexane. A corn oil blank was prepared the same way. This solution was then run on the GC-FID for quantification. The major peak determined during the purity analysis of fenarimol was used for this analysis. Continuing calibration verification (CCV) samples were analyzed to demonstrate on-going calibration accuracy.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a GC-FID purity scan on the fenarimol. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for fenarimol and several very small peaks. The area of the fenarimol peak was 99.7% of the total area of all peaks in the chromatogram. Chemical purity of fenarimol determined by the manufacturer was 99.5% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 08/22/02. Chemical concentration was determined 12 times from 08/22/02 to 11/14/02. The analytical and quality control (QC) results are presented in Appendix C. A single preparation blank was analyzed with every batch for quality control purposes. There were no detectable concentrations of fenarimol in the blanks with the exception of one blank on 08/29/02 with a reported concentration of 209 µg/mL . CCV results ranged from 71.0% to 121%. Internal standards were analyzed with each sample and these results ranged from 91.5% to 113%. The MDL was 115 µg/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg as required for biological testing (Appendix C). The average peroxide number in the Mazola corn oil was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively.

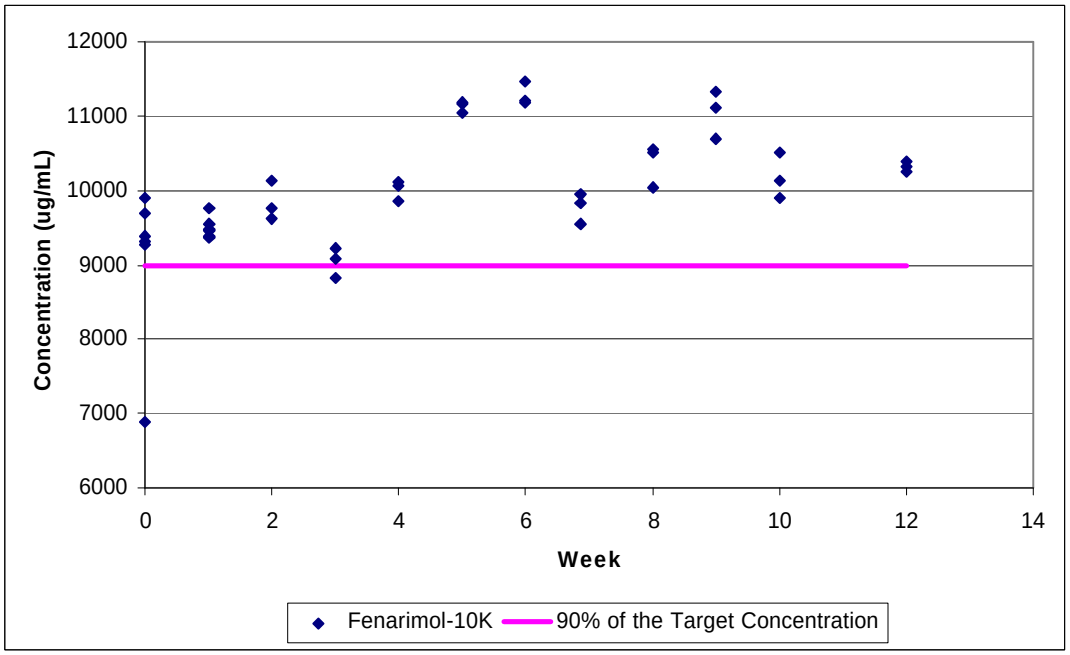
3.3 Statistical Results of Stability Trial

A plot of fenarimol with a target concentration of 10,000 µg/mL against time suggests very little chemical decay (Figure 2). Only one data point during the 09/12/02 (Week 3) analyses was less than 90% of the target concentration. Homogeneity of the chemical concentration within the test container was evaluated at time 0 and at 1 week. At neither time was a significant difference detected ($\alpha = 0.05$) between the concentrations obtained from the top and bottom sections of the container. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of fenarimol was expected to stay greater than or equal to 90% of the target concentration for an unlimited time (Table 3). Thus, this stock solution was considered stable for the required 12-week testing/holding period. The complete statistical analysis is presented in Appendix D.

Observations of fenarimol associated with the target concentration of 50,000 µg/mL showed most samples were at or above 90% of the target concentration through the 6^{th} week of sampling (Figure 2). After 6 weeks, concentrations began to fall below 90% of the target concentration. Homogeneity of the chemical concentration within the test container was evaluated at time 0 and at 1 week. At neither time was a significant difference detected ($\alpha = 0.05$) between the concentrations obtained from the top and bottom sections of the container. One large concentration of 62530 µg/mL observed at time 0 was removed from the analysis and the resulting average day 0 concentration was tested for stability. Based on the final regression model and the lower 95% confidence limit of the slope, the 50,000 µg/mL concentration of fenarimol was expected to stay greater than or equal to 90% of the target concentration for an estimated 6 weeks (Table 3). Thus, this stock solution was considered stable for only 6 weeks of the required 12 week holding time. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries based on target concentrations for all doses ranged from 99.8% to 116%. The complete analysis is presented in Appendix E.



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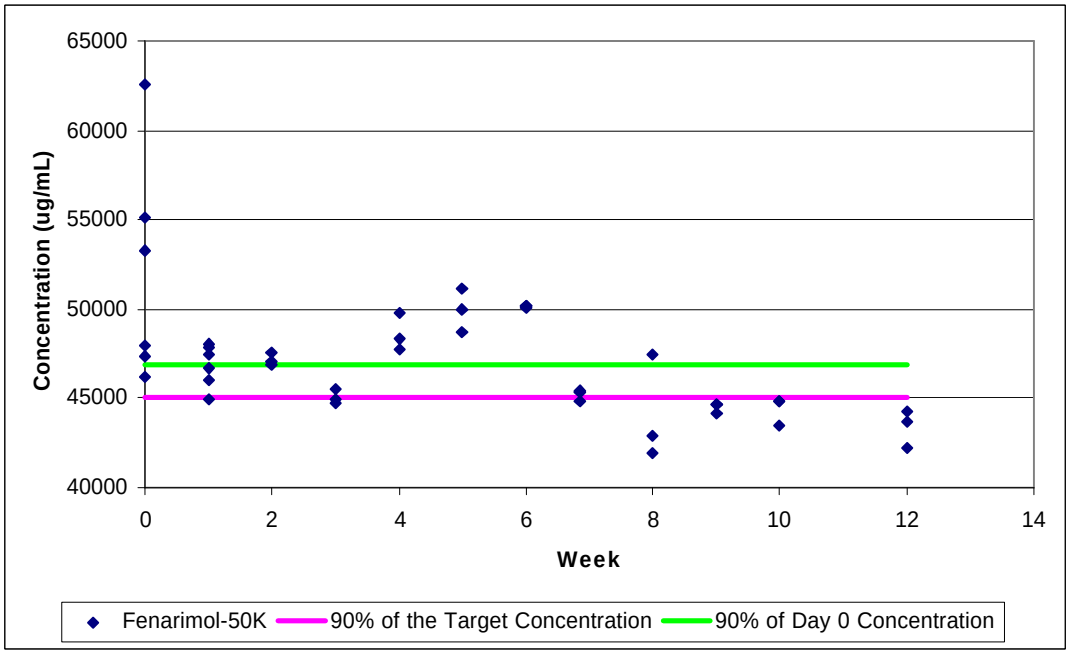


B

Figure 2. Observed Concentration of Fenarimol With a Target Concentration of 10,000 mg/mL (A) and 50,000 mg/mL (B) Against Time

Table 3. Summary of Statistical Results for Fenarimol

WA-2-14-02 **Statistical Analysis conducted by Valerie Cullinan** **Using Minitab Version 13.32, Minitab Inc., 1999.**	**1829-1-2** **Fenarimol-10K**	**1829-1-3** **Fenarimol-50K**
Target Concentration (ug/mL)	10000	50000
Number of determinations	1	1
Number of weeks tested	12	12
Number of replicates per day	3	3
Number of outliers removed	0	1
Number of observations removed	0	0
Overall Mean Concentration	10010	46794
95% Upper CL	10230	47453
error degrees of freedom	41	40
1-sample t-test of Ho: μ >= Target	NS [a]	S
estimated intercept of ln(concentration) against time	9.1448	10.7957
estimated slope of ln(concentration) against time	0.0129	-0.0088
standard error of slope	0.0031	0.0021
error degrees of freedom	40	39
Significance test of lack-of-fit for final model	S [b]	S
Significance test of Ho: β = 0 vs. H1: β ? 0	S	S
Lower 95% CL	0.0067	-0.013
Upper 95% CL	0.0192	-0.005
Maximum Percent Loss (using LCL)	-5.5%	9.9%
Mean Percent Loss (using bhat)	-10.9%	6.8%
LN(90% of Target)	9.1050	10.7144
Number of weeks until at 90% of Target (using LCL)	NA	6
Conclusion:	**Stable for 12 wks**	**Stable for 6 wks**
Average Day 0 Concentration (without outlier)		49962
LN(90% of Day 0 Concentration)		10.7137
Number of weeks until at 90% of Day 0 Concentration (using LCL)		6
Conclusion:		**Stable for 6 wks**

[a] Not Significant at α = 0.05
[b] Significant at α = 0.05

4.0 CONCLUSIONS

Chemical purity of fenarimol as determined by the manufacturer was 99.5%; purity determined by Battelle-Sequim was 99.7%. Stability testing of fenarimol in Mazola corn oil concluded that the chemical was stable at 10 mg/mL for a period of at least 12 weeks, and stable at 50 mg/mL concentrations for a period of 6 weeks.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries based on target concentrations for all doses ranged from 99.8% to 116%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

660 Tower Lane • P.O. Box 599 • West Chester, PA 19381-0599
1-800-452-9994 • 1-610-692-3026 • Fax 1-610-692-8729
info@chemservice.com • www.chemservice.com

CERTIFICATE OF ANALYSIS

INVOICE #: CS229742
PO #: 11120453EAC

CATALOG #: PS-1073 CAS #: 60168-88-9

DESCRIPTION: Fenarimol

LOT #: 287-5B

PURITY: 99.5%

EXPIRATION DATE: 06/07

Chem Service, Inc. guarantees the purity of this chemical ± 0.5% deviation prior to the expiration date shown on the label and exclusive of any customer contamination.

Two or more of the following methods of analysis are used to determine purity: Melting point, refractive index, titration, IR, TLC, GC/FID, GC/TCD, GC/ECD, GC/MS, HPLC or DSC.

Our standards are suitable for use with all EPA methods.

Certified By:

John Conrad

John Conrad
CSM/TC

ISO 9001

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Fenarimol

Chemical Name: Fenarimol (MSL CF Login 1829), CMS 174299

CAS Number: 60168-88-9

Lot Number: 287-5B, stored at RT in Bldg5 Rm 219

Expiration date: 6/07

Manufacturer's Purity Information: 99.5%

Manufacturer's Stability Information: Stable

MSL Purity Results:
Purity (%) To be determined at MSL by GC-FID scan

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Fenarimol

CAS: 60168-88-9

Carrier(s): Mazola corn oil

Concentrations/Dilution Series: 10 and 50 mg/mL

Below MDL determined in Purity Analysis?

In vitro or in *vivo tests*? *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Planned/Proposed testing/holding duration: 12 weeks

EDSP Purity Analysis and Stability Testing Plan for Fenarimol, Continued

Design of Stability Test: Two concentrations, 10.0 mg/mL and 50.0 mg/mL in Mazola corn oil, will be tested. The chemical will be sieved through an 80 mesh screen and material that passes will be suspended in Mazola corn oil with a magnetic stirrer. Samples of the suspension will be taken with a gavage needle, while the suspension is being vigorously stirred, at mid-depth in a 250 mL amber glass bottle, except for the first sampling, which will be sampled at 25% and 75% depth in triplicate to demonstrate homogeneity. The suspension will be stored in glass at 4 deg. C in the dark for 12 weeks, sampled weekly or biweekly in triplicate and analyzed monthly by GC detector.

Number of replicates: 3

Duration: 12 weeks, sampling every week or two so that 8 time points are produced with triplicate samples taken each time

Other factors:

Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:

Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
    - Chemical repository confirmatory test results of chemical identity and purity;
    - Chemical repository test results of lot-to-lot variation in chemical purity;
    - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. Fenarimol concentration in Mazola Corn Oil (µg/mL)

Target Conc.	Sample Name	Date	Fenarimol	Average	RSD	Recovery
10000 ug/ml	1829-1-2-1 top R-1	8/22/2002	6889			
10000 ug/ml	1829-1-2-1 top R-2	8/22/2002	9322	8534	16.7%	85.3%
10000 ug/ml	1829-1-2-1 top R-3	8/22/2002	9389			
10000 ug/ml	1829-1-2-1 bottom R-1	8/22/2002	9898			
10000 ug/ml	1829-1-2-1 bottom R-2	8/22/2002	9696	9618	3.39%	96.2%
10000 ug/ml	1829-1-2-1 bottom R-3	8/22/2002	9260			
50000 ug/ml	1829-1-3-1 top R-1	8/22/2002	62530			
50000 ug/ml	1829-1-3-1 top R-2	8/22/2002	47327	52013	17.6%	104%
50000 ug/ml	1829-1-3-1 top R-3	8/22/2002	46181			
50000 ug/ml	1829-1-3-1 bottom R-1	8/22/2002	47986			
50000 ug/ml	1829-1-3-1 bottom R-2	8/22/2002	55084	52102	7.07%	104%
50000 ug/ml	1829-1-3-1 bottom R-3	8/22/2002	53235			
Blank	Corn Oil (T=0)	8/22/2002	115 U			
10000 ug/ml	1829-1-2-2 top R-1	8/29/2002	9767			
10000 ug/ml	1829-1-2-2 top R-2	8/29/2002	9356	9526	2.25%	95.3%
10000 ug/ml	1829-1-2-2 top R-3	8/29/2002	9457			
10000 ug/ml	1829-1-2-2 bottom R-1	8/29/2002	9538			
10000 ug/ml	1829-1-2-2 bottom R-2	8/29/2002	9385	9468	0.81%	94.7%
10000 ug/ml	1829-1-2-2 bottom R-3	8/29/2002	9479			
50000 ug/ml	1829-1-3-2 top R-1	8/29/2002	47869			
50000 ug/ml	1829-1-3-2 top R-2	8/29/2002	46697	46848	2.04%	93.7%
50000 ug/ml	1829-1-3-2 top R-3	8/29/2002	45978			
50000 ug/ml	1829-1-3-2 bottom R-1	8/29/2002	47509			
50000 ug/ml	1829-1-3-2 bottom R-2	8/29/2002	48050	46823	3.59%	93.7%
50000 ug/ml	1829-1-3-2 bottom R-3	8/29/2002	44909			
Blank	Corn oil (week 1)	8/29/2002	115 U			
Blank	Corn oil (week 1)	8/29/2002	209			
10000 ug/ml	1829-1-2-3 R-1	9/5/2002	10136			
10000 ug/ml	1829-1-2-3 R-2	9/5/2002	9764	9841	2.70%	98.4%
10000 ug/ml	1829-1-2-3 R-3	9/5/2002	9622			
50000 ug/ml	1829-1-3-3 R-1	9/5/2002	47056			
50000 ug/ml	1829-1-3-3 R-2	9/5/2002	46870	47157	0.74%	94.3%
50000 ug/ml	1829-1-3-3 R-3	9/5/2002	47546			
Blank	Corn oil (week 2)	9/5/2002	115 U			
10000 ug/ml	1829-1-2-4 R-1	9/12/2002	9231			
10000 ug/ml	1829-1-2-4 R-2	9/12/2002	9092	9049	2.28%	90.5%
10000 ug/ml	1829-1-2-4 R-3	9/12/2002	8824			
50000 ug/ml	1829-1-3-4 R-1	9/12/2002	45496			
50000 ug/ml	1829-1-3-4 R-2	9/12/2002	44781	45086	0.82%	90.2%
50000 ug/ml	1829-1-3-4 R-3	9/12/2002	44981			
Blank	Corn oil (week 3)	9/12/2002	115 U			
10000 ug/ml	1829-1-2-5 R-1	9/19/2002	10104			
10000 ug/ml	1829-1-2-5 R-2	9/19/2002	9856	10009	1.34%	100%
10000 ug/ml	1829-1-2-5 R-3	9/19/2002	10069			

Table C1. Continued

Target Conc.	Sample Name	Date	Fenarimol	Average	RSD	Recovery[1]
50000 ug/ml	1829-1-3-5 R-1	9/19/2002	47781			
50000 ug/ml	1829-1-3-5 R-2	9/19/2002	48316	48643	2.19%	97.3%
50000 ug/ml	1829-1-3-5 R-3	9/19/2002	49832			
Blank	Corn oil (week 4)	9/19/2002	115 U			
10000 ug/ml	1829-1-2-6 R-1	9/26/2002	11157			
10000 ug/ml	1829-1-2-6 R-2	9/26/2002	11035	11126	0.72%	111%
10000 ug/ml	1829-1-2-6 R-3	9/26/2002	11187			
50000 ug/ml	1829-1-3-6 R-1	9/26/2002	48760			
50000 ug/ml	1829-1-3-6 R-2	9/26/2002	49986	49962	2.38%	99.9%
50000 ug/ml	1829-1-3-6 R-3	9/26/2002	51140			
Blank	Corn oil (week 5)	9/26/2002	115 U			
10000 ug/ml	1829-1-2-7 R-1	10/3/2002	11190			
10000 ug/ml	1829-1-2-7 R-2	10/3/2002	11453	11286	1.28%	113%
10000 ug/ml	1829-1-2-7 R-3	10/3/2002	11216			
50000 ug/ml	1829-1-3-7 R-1	10/3/2002	50147			
50000 ug/ml	1829-1-3-7 R-2	10/3/2002	50080	50142	0.12%	100%
50000 ug/ml	1829-1-3-7 R-3	10/3/2002	50199			
Blank	Corn oil (week 6)	10/3/2002	115 U			
10000 ug/ml	1829-1-2-8 R-1	10/10/2002	9944			
10000 ug/ml	1829-1-2-8 R-2	10/10/2002	9555	9778	2.05%	97.8%
10000 ug/ml	1829-1-2-8 R-3	10/10/2002	9835			
50000 ug/ml	1829-1-3-8 R-1	10/10/2002	44798			
50000 ug/ml	1829-1-3-8 R-2	10/10/2002	45399	45163	0.71%	90.3%
50000 ug/ml	1829-1-3-8 R-3	10/10/2002	45293			
Blank	Corn oil (week 7)	10/10/2002	115 U			
10000 ug/ml	1829-1-2-9 R-1	10/17/2002	10549			
10000 ug/ml	1829-1-2-9 R-2	10/17/2002	10506	10367	2.70%	104%
10000 ug/ml	1829-1-2-9 R-3	10/17/2002	10044			
50000 ug/ml	1829-1-3-9 R-1	10/17/2002	41978			
50000 ug/ml	1829-1-3-9 R-2	10/17/2002	42925	44108	6.59%	88.2%
50000 ug/ml	1829-1-3-9 R-3	10/17/2002	47419			
Blank	Corn oil (week 8)	10/17/2002	115 U			
10000 ug/ml	1829-1-2-10 R-1	10/24/2002	11107			
10000 ug/ml	1829-1-2-10 R-2	10/24/2002	11317	11036	2.92%	110%
10000 ug/ml	1829-1-2-10 R-3	10/24/2002	10685			
50000 ug/ml	1829-1-3-10 R-1	10/24/2002	44699			
50000 ug/ml	1829-1-3-10 R-2	10/24/2002	44176	44524	0.68%	89.1%
50000 ug/ml	1829-1-3-10 R-3	10/24/2002	44699			
Blank	Corn oil (week 9)	10/24/2002	115 U			
10000 ug/ml	1829-1-2-11 R-1	10/31/2002	10140			
10000 ug/ml	1829-1-2-11 R-2	10/31/2002	10503	10181	2.98%	102%
10000 ug/ml	1829-1-2-11 R-3	10/31/2002	9901.00			
50000 ug/ml	1829-1-3-11 R-1	10/31/2002	44821			
50000 ug/ml	1829-1-3-11 R-2	10/31/2002	44816	44381	1.71%	88.8%
50000 ug/ml	1829-1-3-11 R-3	10/31/2002	43505			

Table C1. Continued

Target Conc.	Sample Name	Date	Fenarimol	Average	RSD	Recovery[1]
Blank	Corn oil (week 10)	10/31/2002	115 U			
10000 ug/ml	1829-1-2-12 R-1	11/14/2002	10258			
10000 ug/ml	1829-1-2-12 R-2	11/14/2002	10379	10322	0.59%	103%
10000 ug/ml	1829-1-2-12 R-3	11/14/2002	10329			
50000 ug/ml	1829-1-3-12 R-1	11/14/2002	43728			
50000 ug/ml	1829-1-3-12 R-2	11/14/2002	44270	43409	2.43%	86.8%
50000 ug/ml	1829-1-3-12 R-3	11/14/2002	42231			
Blank	Corn oil (week 12)	11/14/2002	115 U			

[1] Recovery is relative to the target concentration

U = Not detected at a value greater than the MDL

Table C2. CCV Data for Fenarimol Concentration in Mazola Corn Oil

Time	Sample Name	Fenarimol (mg/mL)	Recovery	PD
T=0	EDSP Mix1 5 ug/ml	4.09	81.8%	18.2%
	EDSP Mix1 5 ug/ml	4.66	93.2%	6.80%
	EDSP Mix1 5 ug/ml	4.72	94.4%	5.60%
	EDSP Mix1 5 ug/ml	4.63	92.6%	7.40%
Week 1	EDSP Mix1 5 ug/ml	3.55	71.0%	29.0%
	EDSP Mix1 5 ug/ml	4.40	88.0%	12.0%
	EDSP Mix1 5 ug/ml	4.52	90.4%	9.60%
	EDSP Mix1 5 ug/ml	4.36	87.2%	12.8%
	EDSP Mix1 5 ug/ml	5.19	104%	3.80%
	EDSP Mix1 5 ug/ml	5.13	103%	2.60%
	EDSP Mix1 5 ug/ml	5.14	103%	2.80%
Week 2	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.16	103%	3.20%
	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
Week 3	EDSP Mix1 5 ug/ml	4.47	89.4%	10.6%
	EDSP Mix1 5 ug/ml	4.84	96.8%	3.20%
	EDSP Mix1 5 ug/ml	4.61	92.2%	7.80%
Week 4	EDSP Mix1 5 ug/ml	4.76	95.2%	4.80%
	EDSP Mix1 5 ug/ml	5.06	101%	1.20%
	EDSP Mix1 5 ug/ml	4.85	97.0%	3.00%
Week 5	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.99	120%	19.8%
	EDSP Mix1 5 ug/ml	5.41	108%	8.20%
Week 6	EDSP Mix1 5 ug/ml	3.77	75.4%	24.6%
	EDSP Mix1 5 ug/ml	6.04	121%	20.8%
	EDSP Mix1 5 ug/ml	6.05	121%	21.0%
Week 7	EDSP Mix1 5 ug/ml	4.79	95.8%	4.20%
	EDSP Mix1 5 ug/ml	5.29	106%	5.80%
	EDSP Mix1 5 ug/ml	5.09	102%	1.80%
Week 8	EDSP Mix1 5 ug/ml	4.80	96.0%	4.00%
	EDSP Mix1 5 ug/ml	5.15	103%	3.00%
	EDSP Mix1 5 ug/ml	5.14	103%	2.80%
Week 9	EDSP Mix1 5 ug/ml	4.53	90.6%	9.40%
	EDSP Mix1 5 ug/ml	5.12	102%	2.40%
	EDSP Mix1 5 ug/ml	4.77	95.4%	4.60%
Week 10	EDSP Mix1 5 ug/ml	4.19	83.8%	16.2%
	EDSP Mix1 5 ug/ml	5.10	102%	2.00%
	EDSP Mix1 5 ug/ml	4.73	94.6%	5.40%
	EDSP Mix1 5 ug/ml	5.31	106%	6.20%
	EDSP Mix1 5 ug/ml	5.36	107%	7.20%
Week 12	EDSP Mix1 5 ug/ml	5.23	105%	4.60%
	EDSP Mix1 5 ug/ml	5.32	106%	6.40%
	EDSP Mix1 5 ug/ml	5.29	106%	5.80%

Text Box C1. Calibration Standard Preparation

Calibration Standard EDSP Mix 1
Calibrations were performed using a five-point calibration curve labeled EDSP Mix 1 A thru E. This mix is used for Atrazine, Fenarimol, p,p'-DDE, Methoxychlor and Vinclozolin analyzed by GC-FID. These standards were made by serial dilutions of standards for each compound. • Atrazine standard was made by weighing 0.0499 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with Methylene chloride and labeled 1826-1-1. • Fenarimol standard was made by weighing 0.0506 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1829B-1. • p,p'-DDE standard was made by weighing 0.0501 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1832-1a-1. • Methoxychlor standard was made by weighing 0.0513 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1808-1-3. • Vinclozolin standard was made by weighing 0.0512 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1779-78. This analysis used an internal standard, in this case 5a androstane, which is made by weighing 0.0511 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane, this is then labeled REP7. The EDSP Mix 1 series (A through E) was made as follows. • Solution A, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 0.02 ml REP7 added to a 10 ml volumetric flask and diluted to the mark with hexane. • Solution B, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution C, 0.25 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution D, 0.1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane. • Solution E, 0.05 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane.

Table C3. Internal Standards Data for Fenarimol in Mazola Corn Oil

Sample Name	Date	5A androstane Recovery
Corn oil	8/22/2002	101%
1829-1-2-1 top R-1	8/22/2002	107%
1829-1-2-1 top R-2	8/22/2002	108%
1829-1-2-1 top R-3	8/22/2002	107%
1829-1-2-1 botm R-1	8/22/2002	109%
1829-1-2-1 botm R-2	8/22/2002	108%
1829-1-2-1 botm R-3	8/22/2002	110%
1829-1-3-1 top R-1	8/22/2002	108%
1829-1-3-1 top R-2	8/22/2002	108%
1829-1-3-1 top R-3	8/22/2002	107%
1829-1-3-1 botm R-1	8/22/2002	107%
1829-1-3-1 botm R-2	8/22/2002	106%
1829-1-3-1 botm R-3	8/22/2002	105%
Corn oil	8/29/2002	101%
1829-1-2-2 top R-1	8/29/2002	109%
1829-1-2-2 top R-2	8/29/2002	110%
1829-1-2-2 top R-3	8/29/2002	109%
1829-1-2-2 botm R-1	8/29/2002	111%
1829-1-2-2 botm R-2	8/29/2002	110%
1829-1-2-2 bottom R-3	8/29/2002	112%
1829-1-3-2 top R-1	8/29/2002	110%
1829-1-3-2 top R-2	8/29/2002	109%
1829-1-3-2 top R-3	8/29/2002	109%
1829-1-3-2 botm R-1	8/29/2002	107%
1829-1-3-2 botm R-2	8/29/2002	106%
1829-1-3-2 botm R-3	8/29/2002	110%
Corn oil	8/29/2002	109%
1829-1-2-2 top R-1	8/29/2002	112%
1829-1-2-2 top R-2	8/29/2002	113%
1829-1-2-2 top R-3	8/29/2002	113%
1829-1-2-2 botm R-1	8/29/2002	112%
1829-1-2-2 botm R-2	8/29/2002	111%
1829-1-2-2 botm R-3	8/29/2002	113%
1829-1-3-2 top R-1	8/29/2002	112%
1829-1-3-2 top R-2	8/29/2002	112%
1829-1-3-2 top R-3	8/29/2002	110%
1829-1-3-2 botm R-1	8/29/2002	108%
1829-1-3-2 botm R-2	8/29/2002	108%
1829-1-3-2 botm R-3	8/29/2002	113%
Corn oil	9/5/2002	100%
1829-1-2-3 R-1	9/5/2002	106%
1829-1-2-3 R-2	9/5/2002	108%
1829-1-2-3 R-3	9/5/2002	109%
1829-1-3-3 R-1	9/5/2002	105%
1829-1-3-3 R-2	9/5/2002	105%
1829-1-3-3 R-3	9/5/2002	108%

Table C3. continued

Sample Name	Date	5A androstane Recovery
Corn oil	9/12/2002	112%
1829-1-2-4 R-1	9/12/2002	102%
1829-1-2-4 R-2	9/12/2002	105%
1829-1-2-4 R-3	9/12/2002	105%
1829-1-3-4 R-1	9/12/2002	102%
1829-1-3-4 R-2	9/12/2002	102%
1829-1-3-4 R-3	9/12/2002	103%
Corn oil	9/19/2002	97.1%
1829-1-2-5 R-1	9/19/2002	100%
1829-1-2-5 R-2	9/19/2002	103%
1829-1-2-5 R-3	9/19/2002	104%
1829-1-3-5 R-1	9/19/2002	100%
1829-1-3-5 R-2	9/19/2002	96.4%
1829-1-3-5 R-3	9/19/2002	97.8%
Corn oil	9/26/2002	101%
1829-1-2-6 R-1	9/26/2002	105%
1829-1-2-6 R-2	9/26/2002	111%
1829-1-2-6 R-3	9/26/2002	106%
1829-1-3-6 R-1	9/26/2002	109%
1829-1-3-6 R-2	9/26/2002	107%
1829-1-3-6 R-3	9/26/2002	106%
Corn oil	10/3/2002	99.2%
1829-1-2-7 R-1	10/3/2002	103%
1829-1-2-7 R-2	10/3/2002	104%
1829-1-2-7 R-3	10/3/2002	103%
1829-1-3-7 R-1	10/3/2002	107%
1829-1-3-7 R-2	10/3/2002	105%
1829-1-3-7 R-3	10/3/2002	105%
Corn oil	10/10/2002	96.6%
1829-1-2-8 R-1	10/10/2002	106%
1829-1-2-8 R-2	10/10/2002	109%
1829-1-2-8 R-3	10/10/2002	108%
1829-1-3-8 R-1	10/10/2002	101%
1829-1-3-8 R-2	10/10/2002	101%
1829-1-3-8 R-3	10/10/2002	99.6%
Corn oil	10/17/2002	96.7%
1829-1-2-9 R-1	10/17/2002	98.3%
1829-1-2-9 R-2	10/17/2002	99.5%
1829-1-2-9 R-3	10/17/2002	107%
1829-1-3-9 R-1	10/17/2002	108%
1829-1-3-9 R-2	10/17/2002	100%
1829-1-3-9 R-3	10/17/2002	98.2%
Corn oil	10/24/2002	98.0%
1829-1-2-10 R-1	10/24/2002	91.5%
1829-1-2-10 R-2	10/24/2002	93.4%
1829-1-2-10 R-3	10/24/2002	100%

Table C.3. continued

Sample Name	Date	5A androstane Recovery
1829-1-3-10 R-1	10/24/2002	101%
1829-1-3-10 R-2	10/24/2002	102%
1829-1-3-10 R-3	10/24/2002	101%
Corn oil	10/31/2002	97.2%
1829-1-2-11 R-1	10/31/2002	98.5%
1829-1-2-11 R-2	10/31/2002	101%
1829-1-2-11 R-3	10/31/2002	99.9%
1829-1-3-11 R-1	10/31/2002	102%
1829-1-3-11 R-2	10/31/2002	102%
1829-1-3-11 R-3	10/31/2002	103%
reruns		
1829-1-3-11 R-1	10/31/2002	97.9%
1829-1-3-11 R-2	10/31/2002	99.1%
1829-1-3-11 R-3	10/31/2002	101%
Corn oil	11/14/2002	101%
1829-1-2-12 R-1	11/14/2002	101%
1829-1-2-12 R-2	11/14/2002	99.3%
1829-1-2-12 R-3	11/14/2002	99.5%
1829-1-3-12 R-1	11/14/2002	98.5%
1829-1-3-12 R-2	11/14/2002	97.6%
1829-1-3-12 R-3	11/14/2002	101%

Table C.4. Peroxide concentration in Mazola Corn Oil (meq/kg)

Sample	Analysis Date	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	09/05/02	0.5	0.005	5.00	0.50		
Mazola Corn Oil Expiration 6-03 R-1	09/05/02	1.9	0.005	5.01	1.90		
Mazola Corn Oil Expiration 6-03 R-2	09/05/02	1.8	0.005	5.36	1.68	1.77	6.41
Mazola Corn Oil Expiration 6-03 R-3	09/05/02	1.8	0.005	5.16	1.74		
Mazola Corn Oil Expiration 1-04 R-1	09/05/02	1.2	0.005	4.92	1.22		
Mazola Corn Oil Expiration 1-04 R-2	09/05/02	1.5	0.005	5.2	1.44	1.34	8.31
Mazola Corn Oil Expiration 1-04 R-3	09/05/02	1.4	0.005	5.13	1.36		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-02
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

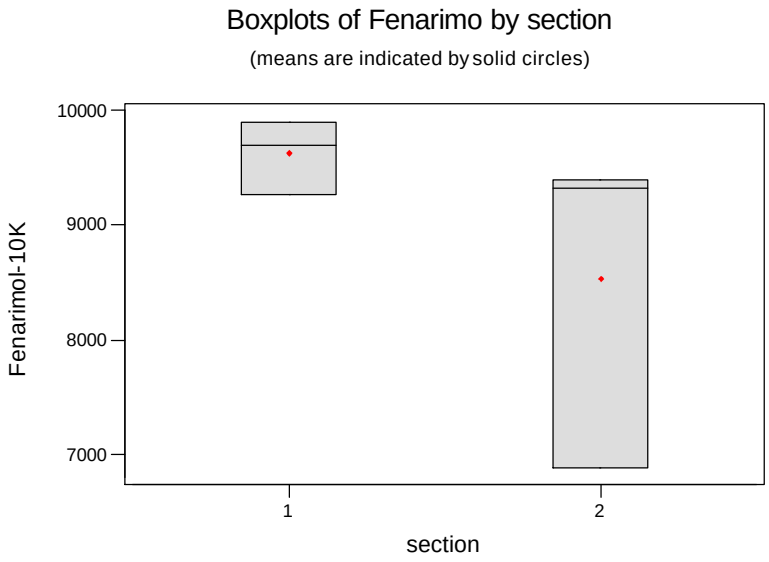
———— 1/24/2003 2:48:30 PM ————————————————————

Results for: Week 0

Two-Sample T-Test and CI: Fenarimol-10K, section

```
Two-sample T for Fenarimol-10K

section     N      Mean     StDev   SE Mean
1           3      9618       326       188
2           3      8534      1425       822

Difference = mu (1) - mu (2)
Estimate for difference:  1084
95% CI for difference: (-2546, 4715)
T-Test of difference = 0 (vs not =): T-Value = 1.29  P-Value = 0.327  DF = 2
```

1 = bottom
2 = top



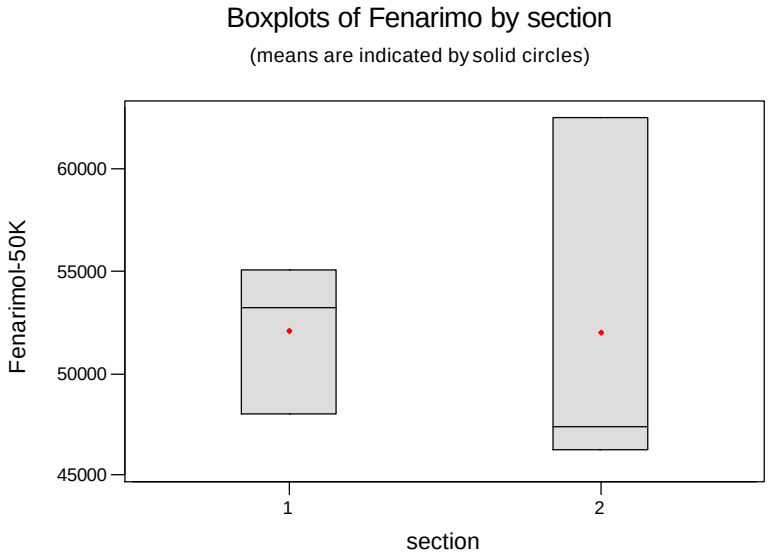
Kruskal-Wallis Test: Fenarimol-10K versus section

```
Kruskal-Wallis Test on Fenarimo

section     N    Median    Ave Rank         Z
1           3      9696         4.3      1.09
2           3      9322         2.7     -1.09
Overall     6                   3.5

H = 1.19  DF = 1  P = 0.275

* NOTE * One or more small samples
```

Can't reject the null that sections are the same.

Two-Sample T-Test and CI: Fenarimol-50K, section

```
Two-sample T for Fenarimol-50K

section     N      Mean     StDev   SE Mean
1           3     52102      3683      2126
2           3     52013      9126      5269

Difference = mu (1) - mu (2)
Estimate for difference:  89
95% CI for difference: (-24358, 24537)
T-Test of difference = 0 (vs not =): T-Value = 0.02  P-Value = 0.989  DF = 2
```



Can't reject the null that sections are the same.

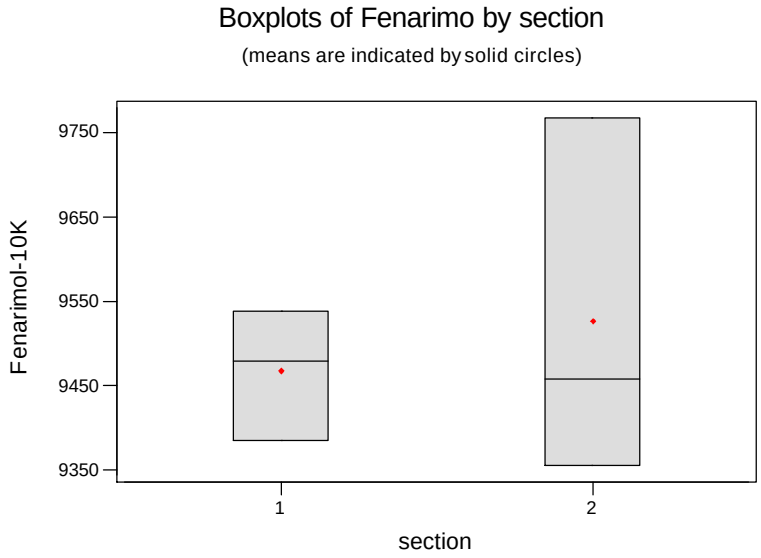
Kruskal-Wallis Test: Fenarimol-50K versus section

```
Kruskal-Wallis Test on Fenarimo

section     N    Median    Ave Rank         Z
1           3     53235         4.0      0.65
2           3     47327         3.0     -0.65
Overall     6                   3.5

H = 0.43  DF = 1  P = 0.513

* NOTE * One or more small samples
```

Results for: Week 1

Two-Sample T-Test and CI: Fenarimol-10K, section

```
Two-sample T for Fenarimol-10K

section     N      Mean     StDev   SE Mean
1           3    9467.6      77.1        44
2           3      9526       214       124

Difference = mu (1) - mu (2)
Estimate for difference:  -59
95% CI for difference: (-624, 507)
T-Test of difference = 0 (vs not =): T-Value = -0.45  P-Value = 0.698  DF = 2
```



Can't reject the null that sections are the same.

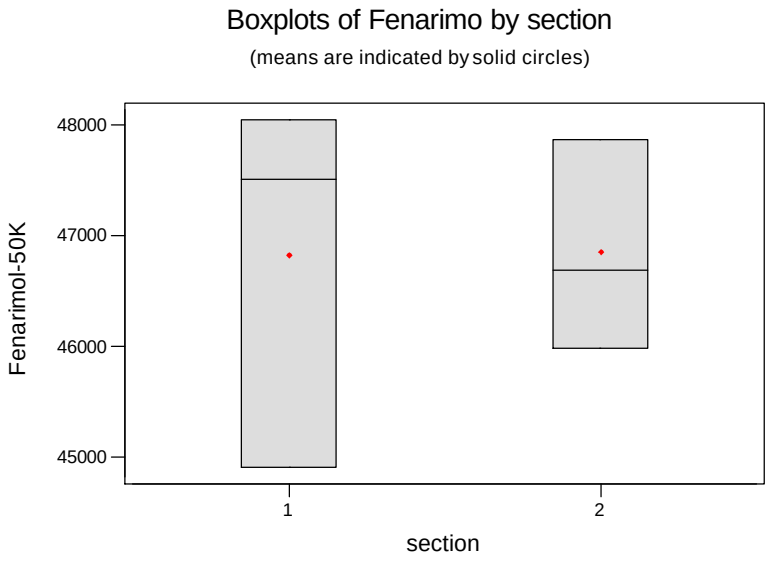
Kruskal-Wallis Test: Fenarimol-10K versus section

```
Kruskal-Wallis Test on Fenarimo

section     N    Median    Ave Rank         Z
1           3      9479         3.7      0.22
2           3      9457         3.3     -0.22
Overall     6                   3.5

H = 0.05  DF = 1  P = 0.827

* NOTE * One or more small samples
```

Two-Sample T-Test and CI: Fenarimol-50K, section

```
Two-sample T for Fenarimol-50K

section     N      Mean     StDev   SE Mean
1           3     46823      1679       969
2           3     46848       955       551

Difference = mu (1) - mu (2)
Estimate for difference:  -25
95% CI for difference: (-3573, 3523)
T-Test of difference = 0 (vs not =): T-Value = -0.02  P-Value = 0.983  DF = 3
```

Boxplots of Fenarimo by section



Can't reject the null that sections are the same.

Kruskal-Wallis Test: Fenarimol-50K versus section

```
Kruskal-Wallis Test on Fenarimo

section     N    Median    Ave Rank         Z
1           3     47509         3.7      0.22
2           3     46697         3.3     -0.22
Overall     6                   3.5

H = 0.05  DF = 1  P = 0.827

* NOTE * One or more small samples
```

Conclusion: All tests between sections have very poor power. For both weeks, no significant differences between the two sections could be detected. Note that Fenarimol-10K is close to being different.

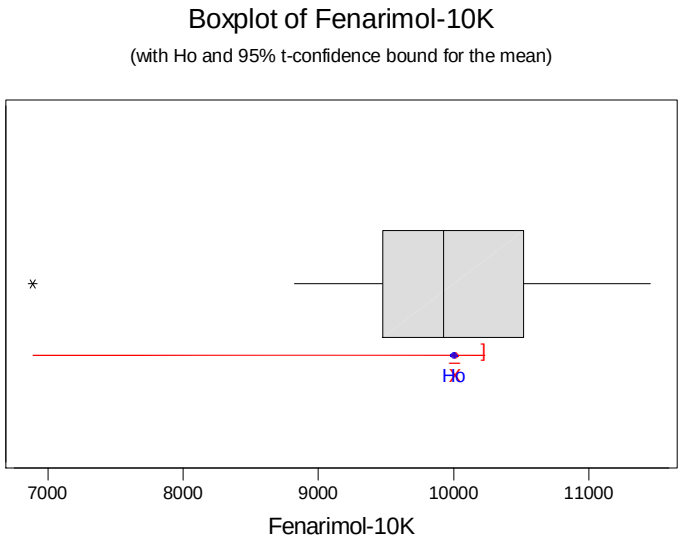
3/4/2003 12:29:24 PM

Stability Data

One-Sample T: Fenarimol-10K

```
Test of mu = 10000 vs mu < 10000

Variable          N      Mean     StDev   SE Mean
Fenarimol-10     42     10010       848       131

Variable      95.0% Upper Bound        T      P
Fenarimol-10              10230     0.08  0.530
```

t Boxplot of Fenarimol-10K



- Outliers are < Median-3*IQD OR > Median+3*IQD

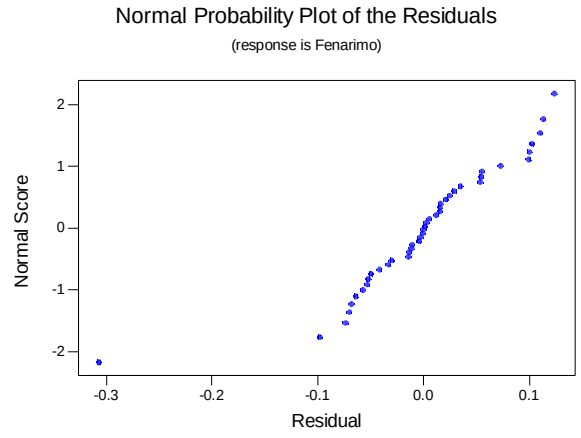
```
Boundary for outliers are values <    6792.54  and >    13052.3
No outliers
```

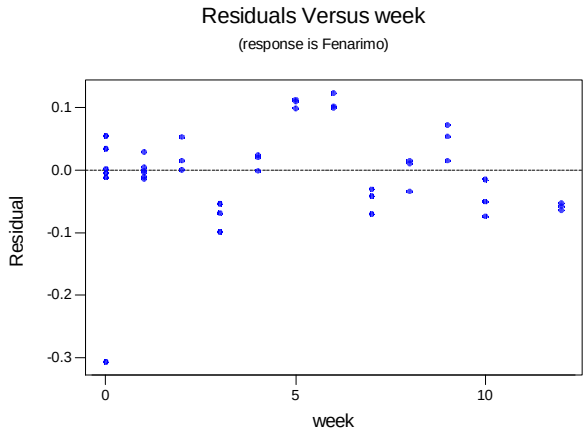
- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	9.2001
0	1	9.1794
0	1	9.1335
0	2	8.8377
0	2	9.1402
0	2	9.1473
1	1	9.1630
1	1	9.1469
1	1	9.1569
1	2	9.1867
1	2	9.1437
1	2	9.1545
2	0	9.2238
2	0	9.1865
2	0	9.1718
3	0	9.1303
3	0	9.1152
3	0	9.0852
4	0	9.2207
4	0	9.1958
4	0	9.2172
5	0	9.3198
5	0	9.3088
5	0	9.3225
6	0	9.3227
6	0	9.3460
6	0	9.3251
7	0	9.2047
7	0	9.1648
7	0	9.1937
8	0	9.2638
8	0	9.2597
8	0	9.2147
9	0	9.3153
9	0	9.3341
9	0	9.2765
10	0	9.2242
10	0	9.2594
10	0	9.2004
12	0	9.2358
12	0	9.2475
12	0	9.2427

- Conducts Simple Linear Regression

```
The regression equation is
Fenarimol-10K = 9.14 + 0.0129 week

Predictor        Coef     SE Coef          T        P
Constant      9.14478     0.01897     482.07    0.000
week         0.012931    0.003083       4.19    0.000

S = 0.07547     R-Sq = 30.5%     R-Sq(adj) = 28.8%

Analysis of Variance
Source            DF          SS          MS         F        P
Regression         1     0.10018     0.10018     17.59    0.000
Residual Error    40     0.22781     0.00570
  Lack of Fit     10     0.12759     0.01276      3.82    0.002
  Pure Error      30     0.10022     0.00334
Total             41     0.32799

Unusual Observations
Obs       week   Fenarimo         Fit      SE Fit    Residual    St Resid
  4        0.0     8.8377      9.1448      0.0190     -0.3071       -4.20R

R denotes an observation with a large standardized residual
```






```
Do you want to remove any data points? (yes OR no)
no
```

```
Should a quadratic be fit? (yes OR no)
no
```

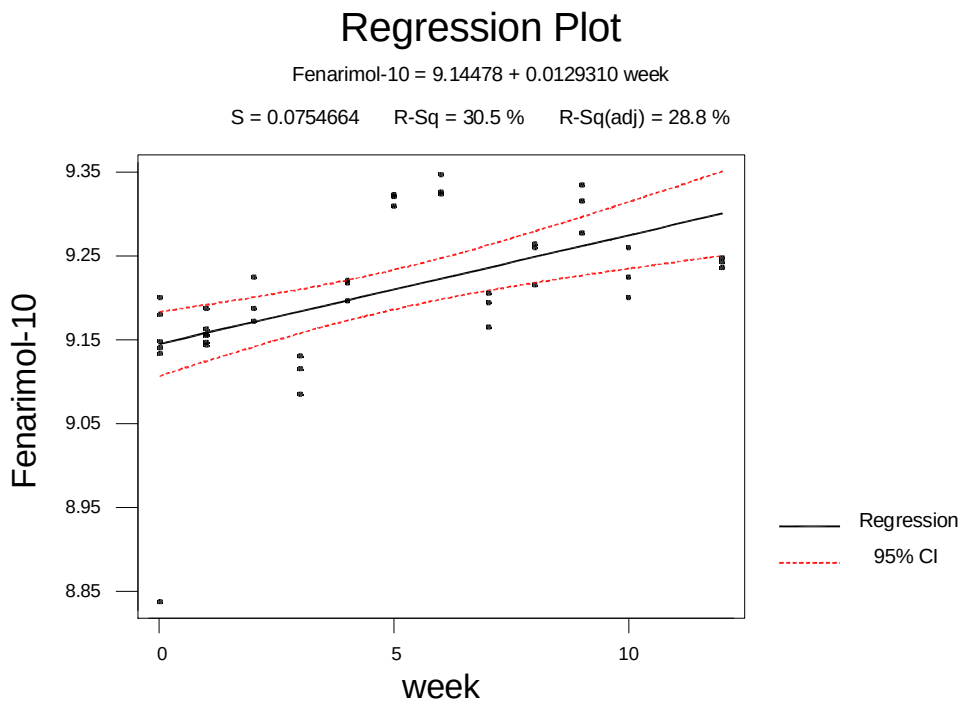
- Power analysis for t-test of slope less than zero

Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.07547

Sample
  Size   Power  Difference
    40  0.9900     -0.0482
```

- That means we would detect a mean of 9.162 as significantly less than ln(10000) = 9.2103 or a change of 9529 from 10000 = 4.7% loss.

- Fit 95% confidence bands about the fitted simple linear model



- **Conclusion – stable for 12 weeks.**

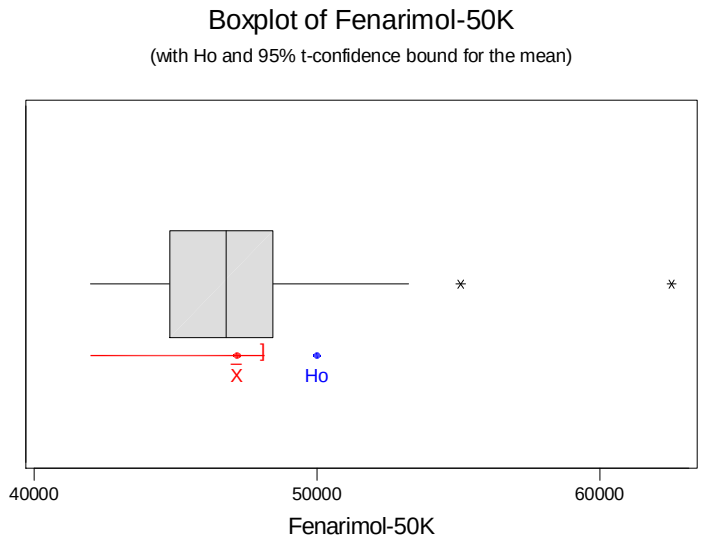
- Performs a one-sample t-test for mu less than TARGET &

```
What is the target value for X    7
DATA> 50000
```

One-Sample T: Fenarimol-50K

```
Test of mu = 50000 vs mu < 50000

Variable          N      Mean     StDev   SE Mean
Fenarimol-50     42     47169      3722       574

Variable      95.0% Upper Bound        T      P
Fenarimol-50              48135    -4.93  0.000
```

t Boxplot of Fenarimol-50K



- Outliers are < Median-3*IQD OR > Median+3*IQD

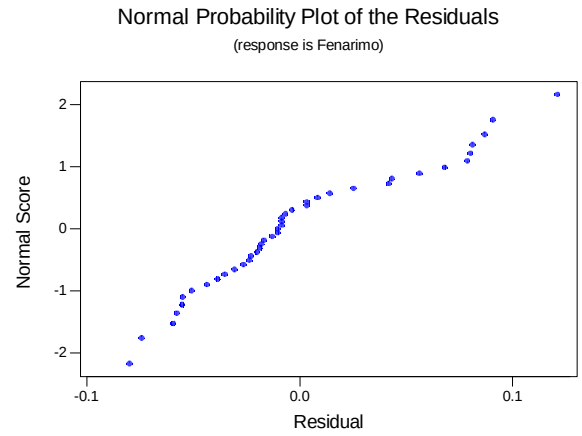
```
Boundary for outliers are values <    35883.4  and >    57683.6
Week  Rep  High Value
  0    2   62530.0

Do you want to remove any outliers? (yes OR no)
yes
How many would you like to remove
DATA> 1
Type which rows to remove
DATA> 4
```

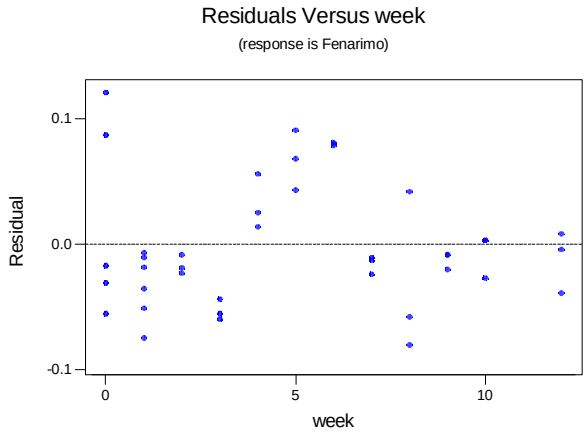
- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	10.7787
0	1	10.9166
0	1	10.8825
0	2	*
0	2	10.7648
0	2	10.7403
1	1	10.7687
1	1	10.7800
1	1	10.7124
1	2	10.7762
1	2	10.7514
1	2	10.7359
2	0	10.7591
2	0	10.7551
2	0	10.7695
3	0	10.7254
3	0	10.7095
3	0	10.7140
4	0	10.7744
4	0	10.7855
4	0	10.8164
5	0	10.7947
5	0	10.8195
5	0	10.8423
6	0	10.8227
6	0	10.8214
6	0	10.8237
7	0	10.7099
7	0	10.7233
7	0	10.7209
8	0	10.6449
8	0	10.6672
8	0	10.7668
9	0	10.7077
9	0	10.6959
9	0	10.7077
10	0	10.7104
10	0	10.7103
10	0	10.6806
12	0	10.6857
12	0	10.6981
12	0	10.6509

- Conducts Simple Linear Regression

```
The regression equation is
Fenarimol-50K = 10.8 - 0.00883 week

41 cases used 1 cases contain missing values

Predictor        Coef     SE Coef          T        P
Constant      10.7957      0.0131     825.36    0.000
week        -0.008833    0.002100      -4.21    0.000
S = 0.05036     R-Sq = 31.2%     R-Sq(adj) = 29.4%

Analysis of Variance
Source            DF          SS          MS         F        P
Regression         1    0.044859    0.044859     17.69    0.000
Residual Error    39    0.098926    0.002537
  Lack of Fit     10    0.058462    0.005846      4.19    0.001
  Pure Error      29    0.040464    0.001395
Total             40    0.143785

Unusual Observations
Obs       week   Fenarimo         Fit      SE Fit    Residual    St Resid
  2        0.0    10.9166     10.7957      0.0131      0.1209        2.49R

R denotes an observation with a large standardized residual
```





```
Do you want to remove any data points? (yes OR no)
no
Should a quadratic be fit? (yes OR no)
No
```

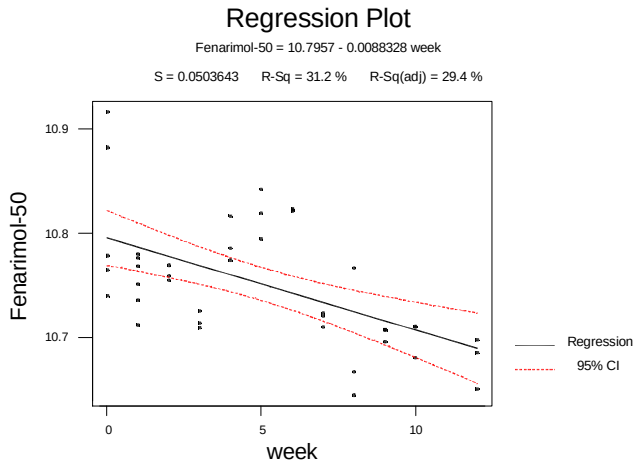
- Power analysis for t-test of slope less than zero

Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.05036

Sample
  Size   Power  Difference
    39  0.9900     -0.0326
```

- That means we would detect a mean of 10.787 as significantly less than ln(50000) = 10.820 or a change of 48396 from 50000 = 3.2% loss.

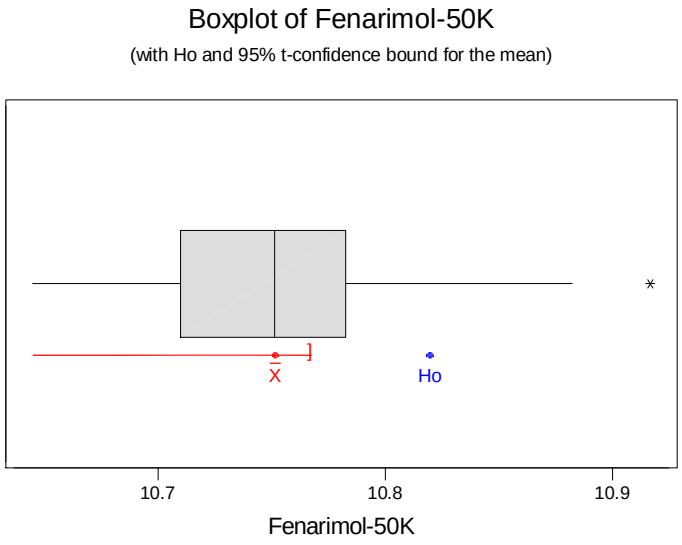
- Fit 95% confidence bands about the fitted simple linear model



- One-sample t-test for mu less than LN(TARGET) after removal of data point

One-Sample T: Fenarimol-50K

```
Test of mu = 10.82 vs mu < 10.82

Variable          N      Mean     StDev   SE Mean
Fenarimol-50     41   10.7517    0.0600    0.0094

Variable      95.0% Upper Bound        T      P
Fenarimol-50            10.7675    -7.29  0.000
```



- **Conclusion – stable for 6 weeks.**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Fenarimol in-life test solution samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Fenarimol suspension in corn oil

TEST SOLUTION SAMPLE CUSTODY AND PROCESSING:

Test solution samples were prepared by the EDSP Chemical Repository, Sequim, WA, using fenarimol (CAS 60168-88-9, CF 1829, Chem Service lot # 287-5B, expiration date 6/07) suspended in Mazola corn oil (corn oil was from containers with the following expiration dates: 6/12/03, 1/1/04, and 4/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time. Samples were prepared at two test concentrations for all replicates and exposures unless noted below; 10 mg/mL and 50 mg/mL. The 10 mg/mL concentration was prepared by suspending 2.0 g of fenarimol in 184 g of corn oil in a pre-cleaned, amber-glass container. The 50 mg/mL concentration was prepared by suspending 10.0 g of fenarimol in 176 g of corn oil. Fenarimol was sieved through an 80-mesh screen prior to use.

Samples for female-only rat exposures were prepared at two different times (Table 1):
Replicate 1 – prepared on 9/9/02 and shipped on 9/10/02
Replicate 2 – prepared on 9/15/02 and shipped on 9/16/02
Note: Replicate 2 was sent as a back-up, and was not analyzed.

The test solution was sampled four times during the female test (9/18/02, 9/24/02, 10/01/02, and 10/08/02) Data are reported in Table 2. Remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test were analyzed and are reported in Table 3.

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:

The container was placed on a magnetic stir plate and stirred. Triplicate 1 mL samples from the top (about 0.25 inches below the surface) and bottom (about 1 inch from the bottom) of the container were sampled and placed in a tared, 30 mL, amber bottle. This aliquot was placed in a 30 mL amber ashed vial (the weight of the sample was determined gravimetrically), and 25 mL of methylene chloride was added and the bottle agitated to mix. Then, 0.1 mL sample and 0.02 mL internal standard, 5a androstane, and 0.88 mL hexane were transferred to an auto sampler vial.

In-life and Returned Container Samples:

For the containers with sufficient material to analyze, the remaining containers were removed from the refrigerator, allowed to warm to room temperature, and

then stirred using a magnetic stir bar and stir plate. About 1 mL was sampled and placed in a tared, 30 mL, amber glass bottle. The weight of the sample was determined gravimetrically. 25 mL of methylene chloride (MeCl) was added and the bottle agitated to mix. For the 10 mg/mL solutions, 0.1 mL was transferred to a 1.8 mL vial with 0.02 mL of internal standard solution containing 5a androstane, and 0.88 mL hexane. For the 50 mg/mL solutions, 0.025 mL was transferred to a 1.8 mL vial with 0.02 mL of internal standard solution containing 5a androstane, and 0.955 mL hexane.

The in-life samples were returned in 20 mL scintillation vials, which contained a slurry with the fenarimol settled to the bottom. The entire sample was extracted to ensure accurate analysis. The vial was weighed and the contents poured into a 60 mL, amber glass bottle. 50 ml of MeCl was used for these samples. The scintillation vial was rinsed with part of the 50 mL of MeCl; this rinse was then poured into the amber vial and this rinsing repeated to ensure complete transfer of the sample. The empty vial was dried and re-weighed. The amber bottles were agitated to mix, and 0.01 mL transferred to an auto sampler vial with 0.02 mL of internal standard solution containing 5a androstane, and 0.97 mL hexane.

SAMPLE ANALYSIS: The samples were analyzed by gas chromatograph (GC) with a flame ionization detector (FID). The GC was set up with an auto sampler and a 30 m x 0.25 mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and the detector temperature at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution.

Data Quality Objectives	**Control Limits**
Procedural Blank	<5 X MDL
Blank Spike Recovery	40% - 120%
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: GC-FID

CALIBRATION: Calibration with a five-point curve was done using standard dilutions prepared from EDSP Mix 1 (see Appendix C) with a continuing calibration verification (CCV) sample analyzed every 10 samples.

CONTINUING STANDARD RECOVERY: Percent recovery results for initial and CCV samples analyzed with the in-life sample data set ranged from 75% to 121% with a mean recovery of 101%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK: Fenarimol was not detected above the detection limit in the corn-oil blank analyzed with the test solution and in-life samples.

DETECTION LIMIT: The fenarimol method detection limit (MDL) in corn oil was 115 µg/mL, as determined by an MDL study. No data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed. In this analysis, sampling was performed by taking the sample material from flask through to analysis. Analyzing a spiked sample would be no different from analyzing a CCV.

INTERNAL STANDARD: 5a androstane was spiked into each sample and analyzed as the internal standard. Average percent recovery results were 96% and ranged from 79% to 111%. There were no cases in which the percent recovery of the internal standard exceeded the acceptance range of 40% to 120%.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSDs) for the two test solutions ranged from 1.79 to 3.84.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of Fenarimol Formulation Concentrations Prepared 09/09/02

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	%RSD
R-1; 09/09/02				
10 mg/mL	2-14-F-F Top R-1Fen	9.19		
10 mg/mL	2-14-F-F Top R-2Fen	9.18	9.29	2.01
10 mg/mL	2-14-F-F Top R-3Fen	9.51		
10 mg/mL	2-14-F-F Bot R-1Fen	9.37		
10 mg/mL	2-14-F-F Bot R-2Fen	9.04	9.23	1.79
10 mg/mL	2-14-F-F Bot R-3Fen	9.27		
50 mg/mL	2-14-G-F Top R-1Fen	44.1		
50 mg/mL	2-14-G-F Top R-2Fen	44.8	45.2	3.14
50 mg/mL	2-14-G-F Top R-3Fen	46.8		
50 mg/mL	2-14-G-F Bot R-1Fen	44.5		
50 mg/mL	2-14-G-F Bot R-2Fen	47.5	46.6	3.84
50 mg/mL	2-14-G-F Bot R-3Fen	47.7		

Table 2. Fenarimol In-life Samples

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
09/18/02	10/16/02	06/04/03	10 mg/mL	WA2-14F-F 9-18 Vial	10.91	109%
09/24/02	10/16/02	06/05/03	10 mg/mL	WA2-14F-F 9-24 Vial	10.95	109%
10/01/02	10/16/02	06/05/03	10 mg/mL	WA2-14F-F 10-1 Vial	11.17	112%
10/08/02	10/16/02	06/05/03	10 mg/mL	WA2-14F-F 10-8 Vial	11.55	116%
09/18/02	10/16/02	06/04/03	50 mg/mL	WA2-14G-F 9-18 Vial	49.88	99.8%
09/24/02	10/16/02	06/05/03	50 mg/mL	WA2-14G-F 9-24 Vial	54.63	109%
10/01/02	10/16/02	06/05/03	50 mg/mL	WA2-14G-F 10-1 Vial	54.70	109%
10/08/02	10/16/02	06/05/03	50 mg/mL	WA2-14G-F 10-8 Vial	55.59	111%

Table 3. Fenarimol Post-Test Sample Concentrations for Formulations Returned to Battelle from RTI

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
09/15/02	10/16/02	11/22/02	10 mg/mL	WA 2-14-F-F Rep2Jar	9.98	100%
09/15/02	10/16/02	11/22/02	50 mg/mL	WA 2-14-G-F Rep2Jar	51.0	102%

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-004: Atrazine, DDE, vinclozolin, Methoxychlor, Fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[X]	Protocol
[ ]	SOP	[ ]	Method	[ ]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: 2.3 of protocol WA 2-14 states "an aliquot of each level per formulation will be analyzed"

DEVIATION: Each dose level was tested in the first preparation for each chemical. However, subsequent batches were not always analyzed.

REASON/IMPACT: No impact. Subsequent batches were prepared using the same methods and procedures as the first batches.
PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action required.

ACTIONS TO PREVENT RECURRENCE: Upper management will review the analyses schedule prior to the start of the studies.

Approval:

Michael Blanton,
WAL — Date 11-3-03

Eric Crecelius,
Study Director
Chemical Repository — Date 11-3-03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Ketoconazole in Mazola Corn Oil

November 3, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory

1529 West Sequim Bay Road

Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology

Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Ketoconazole in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Ketoconazole in Mazola Corn Oil

Parameter	Chemical
Compound Name	Ketoconazole
CAS #	65277-42-1
Central File No.	CF-1850
Initial Receipt Date	6/21/02
Expiration Date	9/30/2005
Manufacturer	Spectrum Laboratory Products, Inc.
Lot Number	QL0352
Battelle Study #	WA 2-14-02-02
Method	SW 846, 8316 Modified

Executive Summary

The chemical purity of ketoconazole determined by the manufacturer was 99.7%. The purity result from Battelle-Sequim by HPLC was determined to be 100%. During stability testing, all but two data points were greater than the target concentration of 10 mg/mL. Thus, the average day 0 concentration of 11.3 mg/mL was tested for stability. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of ketoconazole was expected to stay greater than or equal to 90% of the day 0 concentration for up to an estimated 8 weeks. Thus, stability testing of the ketoconazole stock solution in corn oil was considered stable at the average day 0 concentration of 11.3 mg/mL concentration for only 8 weeks of the required testing and holding period of 12 weeks.

Mazola corn oil (expiration dates 6/03 and 1/04) was purchased from local grocery stores, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 9/5/02 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn oil with an expiration date of 6/03 was 1.77 meq/kg (RSD = 6.41%). The average peroxide number in the Mazola corn oil with an expiration date of 1/04 was 1.34 meq/kg (RSD = 8.31%). This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses ranged from 58% to 109%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA 2-14-02-02, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of ketoconazole (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_Ketoconazole-cornoil.doc, PSTP_WA-2-14_Ketoconazole_cornoil.doc, DSUM_WA-2-14_Ketoconazole-crnoil.xls, and DAF_WA-2-14_Ketoconazole-crnoil.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, ketoconazole, (CAS No. 65277-42-1) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Ketoconazole was purchased from Spectrum Laboratory Products, Inc. and lot number QL0352 was initially received on 6/21/02 with an expiration date of 9/30/2005 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1850) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Corn oil (expiration dates 6/03 and 1/04) was purchased from local grocery stores, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 9/5/02 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-02

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Ketoconazole (MSL CF 1850)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 10 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Testing/holding duration: 12 weeks

Chemical Information

Chemical Name: Ketoconazole

CAS: 65277-42-1

Any known purity information: may refer to attached documentation
Manufacturer's Purity Information: 99.7% pure
Any known stability information: may refer to attached documentation
Manufacturer's Stability Information: stable
Desired purity (%) for test? 95% or greater

Figure 1. EDSP Requisition Form for Ketoconazole

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Ketoconazole
CAS #	65277-42-1
Central File No.	CF-1850
Initial Receipt Date	6/21/2002
Expiration Date	9/30/2005
Manufacturer	Spectrum Laboratory Products, Inc.
Lot Number	QL0352
Manufacturer's Purity	99.7%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA 2-14-02-02
Method	SW 846, 8316 Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted on a high performance liquid chromatography (HPLC) with ultraviolet (UV) absorbance at 245 nm. For analysis, 0.1009 grams of the ketoconazole was weighed into a 100 mL volumetric flask and diluted to the 100 mL mark with acetonitrile (ACN), labeled PP-1198. Next, 0.5 mL of this solution was transferred to another 100 mL volumetric flask and diluted to the 100 mL mark with a 70% Acetonitrile:30% 50mM phosphate buffer, labeled PP-1199A. This standard was run and compared to a blank ACN:water (60% ACN:40% deionized water) solution. These matrices were run on the HPLC and the purity determined by comparing the peak heights of the peaks in the chromatogram. The area of the ketoconazole peak was compared to all the peaks in the chromatogram after the blank peak areas were subtracted. The HPLC was set up with an auto sampler and a column oven. The column oven temperature was set at 30ºC, and the auto sampler was set to inject 200 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. A stock solution was prepared to arrive at the chemical concentration requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

A ketoconazole stock matrix was prepared on 10/23/02 for testing as described in Table 2. Briefly, for the 10 mg/mL ketoconazole, 2.0 g was weighed into a wide-mouth amber glass bottle and 184 g of corn oil was added. The sample was stirred and stored in a refrigerator. Time 0 (T=0) samples were collected on 10/24/02 from the top and bottom of the container in

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA 2-14-02-02 12 Weeks	Ketoconazole	10 mg/mL	1850-1-2	2.0 g in 184 g Mazola corn oil

triplicate to assess mixing homogeneity. A corn oil blank sample was also collected. The bottle was labeled and stored at 4ºC ± 2ºC for the duration of the test.

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by chromatographic analysis. Triplicate aliquots were tested for the 10 mg/mL concentration. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

Ketoconazole stock solution was sampled for stability testing by removing the solution from the refrigerator, allowing it to warm to room temperature, and then stirring it overnight. Then, triplicate 1 mL samples were sampled and placed in a tared 60 mL amber bottle. The sample weight was determined gravimetrically. Then 50 mL ACN (JT Baker lot # 448346) was added and the container agitated. Then, 0.01 mL was transferred to an auto sampler vial with 0.99 mL 60% ACN in water. This solution was analyzed on the HPLC using a UV/VIS detector at the 245 nm wavelength. A 70:30% ACN:water buffer was used as an eluent at 1.5 mL/min. The eluent was made by adding 75 mL buffer (50 mM phosphate with pH adjusted to 7 with sodium hydroxide (NaOH), 75 mL DI water and 350 mL ACN. Separation was attained using a Supelco PAH column (a C-18 column). Calibration was done using standard PP-1191 with a 5-point calibration curve for samples analyzed from 10/24/02 to 11/14/02. Given the high recoveries observed with these samples, a new calibration standard (PP-1199) was created on 11/18/02 and this standard and associated 5-point curve were used to calculate the concentrations for samples collected and analyzed from 11/19/02 to 1/16/03. HPLC run data were stored on computer WV04738. A multiplier of 5000 was used in the STAR software (50 mL ACN/ 0.01 mL sample). A corn oil blank was analyzed with the samples. The major peak determined during the purity analysis of ketoconazole was used for this analysis. Continuing calibration verification (CCV) samples were analyzed to demonstrate on-going calibration accuracy.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a HPLC purity scan on the ketoconazole. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for ketoconazole and several very small peaks. The area of the ketoconazole peak was 100% of the total area of all peaks in the chromatogram. Chemical purity of ketoconazole determined by the manufacturer was 99.7% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 10/24/2002. Chemical concentration was determined 10 times over a period of 12 weeks. The analytical and QC results are presented in Appendix C. A single preparation blank was analyzed with every batch for quality control purposes. There were no detectable concentrations of ketoconazole in the blanks. CCV results ranged from 92.0% to 111%. Internal standards were not analyzed. The MDL was 252,250 ng/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg as required for biological testing (Appendix C). The average peroxide number in the Mazola corn oil with an expiration date of 6/03 was 1.77 meq/kg (RSD = 6.41%). The average peroxide number in the Mazola corn oil with an expiration date of 1/04 was 1.34 meq/kg (RSD = 8.31%).

3.3 Statistical Results of Stability Trial

A plot of ketoconazole with a target concentration of 10,000,000 ng/mL against time shows a potential decay in concentration (Figure 2). Homogeneity of the chemical concentration was tested at time 0. Because one sample from both the top and bottom sections of the container was about the same concentration, no difference could be detected. Over the 12 week testing period all but two data points were greater than the target concentration. Thus, the average day 0 concentration was used to test stability. Only two data points were less than 90% of the average day 0 concentration, however a significant ($p < 0.001$) decrease in concentration was observed. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of ketoconazole was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 8 weeks (Table 3). Thus, this stock solution was considered stable for only 8 weeks of the required 12-week testing/holding period. It should be noted that the observed decay in concentration could be an artifact of the change in the calibration standard. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses ranged from 58% to 109%. The complete analysis is presented in Appendix E.

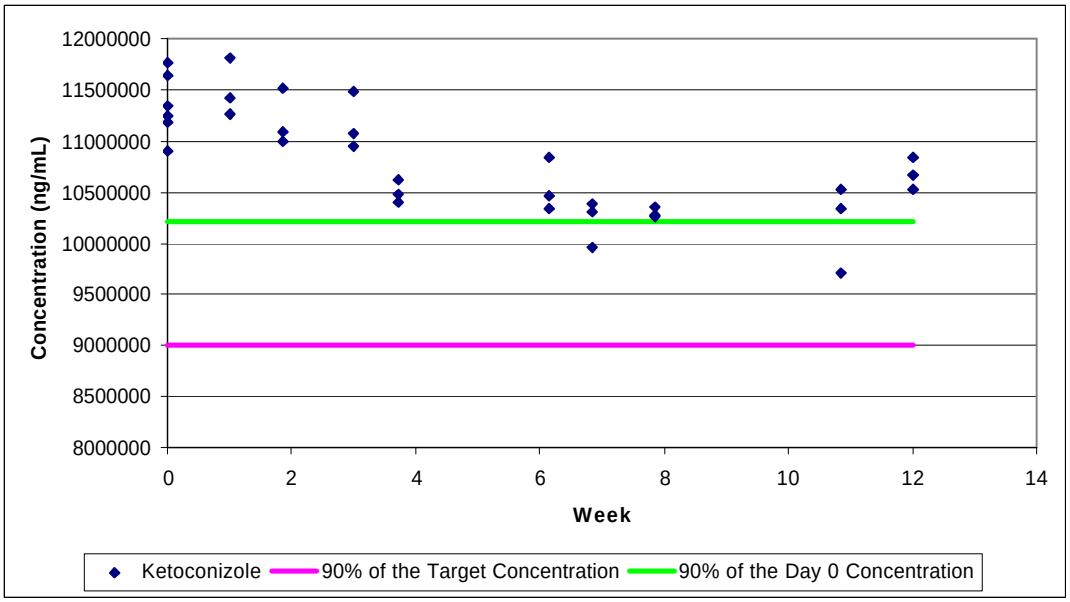

Figure 2. Observed Concentration of Ketoconazole with a Target Concentration of 10,000,000 ng/mL Against Time

Table 3. Summary of Statistical Results for Ketoconazole

WA 2-14-02 Statistical Analysis conducted by Valerie Cullinan Using Minitab Version 13.32, Minitab Inc., 1999.	1850-1-2 Ketoconazole
Target Concentration (ng/mL)	10000000
Number of determinations	1
Number of weeks tested	12
Number of replicates per week	3
Number of outliers removed	0
Number of observations removed	0
Overall Mean Concentration	10816801
95% Upper CL	10974792
Error degrees of freedom	32
1-sample t-test of Ho: μ >= Target	NS [a]
Estimated intercept of ln(concentration) against time	16.2393
Estimated slope of ln(concentration) against time	-0.0089
Standard error of slope	0.0015
Error degrees of freedom	31
Significance test of lack-of-fit for final model	S [b]
Significance test of Ho: β = 0 vs. H1: β ? 0	S
Lower 95% CL of β	-0.012
Upper 95% CL of β	-0.006
Maximum Percent Loss (using LCL)	9.1%
Mean Percent Loss (using bhat)	6.9%
LN(90% of Target)	16.0127
Number of weeks until at 90% of Target (using LCL)	19
Conclusion using Target Concentration:	**Stable for 12 wks**
Average Day 0 Concentration	11346232
LN(90% of Day 0 Concentration)	16.1390
Number of weeks until at 90% of Day 0 Concentration (using LCL)	8
Conclusion using Day 0 Concentration:	**Stable for 8 wks**

[a] Not Significant at α = 0.05
[b] Significant at α = 0.05

4.0 CONCLUSIONS

The chemical purity of ketoconazole determined by the manufacturer was 99.7%. The purity result from Battelle-Sequim by HPLC was determined to be 100%. Stability testing of ketoconazole in corn oil concluded that the chemical was stable at the 10 mg/mL concentration for only a period of 8 weeks out of the required 12 week biological testing period.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses ranged from 58% to 109%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

CERTIFICATE OF ANALYSIS

Date: 06/19/02

PRODUCT: KETOCONAZOLE USP

CATALOG NO: K1149 **
LOT NO: QL0352

CUSTOMER P.O.: 2581

CUSTOMER NO: GSA772
COUNTRY OF ORIGIN: SA
MANUFACTURER: SPECTRUM

DESCRIPTION	LIMIT MIN.	LIMIT MAX.	RESULT
ASSAY (DRIED BASIS)	98.0	102.0 %	99.73 %
MELTING RANGE	148	152 C	149 - 150 C
SPECIFIC ROTATION $[\alpha]_D$	-1 to	+1	-0.786
LOSS ON DRYING	–	0.5 %	0.22 %
RESIDUE ON IGNITION	–	0.1 %	0.05 %
HEAVY METALS	–	0.002 %	<0.002 %
CHROMATOGRAPHIC IMPURITIES	– TO PASS TEST		PASSES TEST
ORGANIC VOLATILE IMPURITIES	– TO PASS TEST		PASSES TEST
IDENTIFICATION	– TO PASS TEST		PASSES TEST
EXPIRATION DATE			09/30/2006

APPROVED BY:

Lilian D. Casabar

LILIAN D. CASABAR
CofA COORDINATOR
New Brunswick, N.J. Plant

encl 194

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APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Ketoconazole

Chemical Name: Ketoconazole (MSL CF 1850)

CAS Number: 65277-42-1

Lot Number: QL0352, stored at RT in MSL5, Rm 219

Expiration date: 9/30/2005

Manufacturer's Purity Information: 99.7%

Manufacturer's Stability Information: stable

MSL Purity Results:
Purity (%) To be determined at MSL by LC or UV-VIS scan

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Ketoconazole

CAS: 65277-42-1

Carrier(s): suspended in Mazola corn oil

Concentrations/Dilution Series: 10 mg/mL

In vitro or in *vivo tests*? *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Testing/holding duration: 12 weeks

Design of Stability Test: One concentration of Ketoconazole, 10 mg/mL in Mazola corn oil, will be tested. The chemical will be sieved through an 80 mesh screen and material that passes will be suspended in Mazola corn oil with a magnetic stirrer. Samples of the suspension will be taken with a gavage needle, while the suspension is being vigorously stirred, at mid-depth in a 250 mL amber glass bottle, except for the first sampling, which will be sampled at 25% and 75% depth in triplicate to demonstrate homogeneity. The suspension will be stored in glass at 4 deg. C in the dark for 12 weeks, sampled at least 8 times in triplicate and analyzed monthly by UV-VIS.

Number of replicates: 3

Duration: 12 weeks, sampling at least 8 time points with triplicate samples taken each time

Other factors:
Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other: None

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:
Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
  - Chemical repository confirmatory test results of chemical identity and purity;
  - Chemical repository test results of lot-to-lot variation in chemical purity;
  - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- Dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. Ketoconazole concentration in Mazola Corn Oil (ng/mL)

Target Conc.	Sample ID	Date	Ketoconazole	Average	RSD	Recovery[1]
Blank	1850-1-2 Blank 1	10/24/2002	252250 U			
10000000 ng/ml	1850-1-2-1 Top R-1	10/24/2002	11177361			
10000000 ng/ml	1850-1-2-1 Top R-2	10/24/2002	11335902	11138266	1.97%	111%
10000000 ng/ml	1850-1-2-1 Top R-3	10/24/2002	10901535			
10000000 ng/ml	1850-1-2-1 Bott R-1	10/24/2002	11641456			
10000000 ng/ml	1850-1-2-1 Bott R-2	10/24/2002	11769411	11554197	2.33%	116%
10000000 ng/ml	1850-1-2-1 Bott R-3	10/24/2002	11251724			
Blank	1850-1-2 Blank 2	10/31/2002	252250 U			
10000000 ng/ml	1850-1-2-2 R-1	10/31/2002	11261977			
10000000 ng/ml	1850-1-2-2 R-2	10/31/2002	11809165	11495240	2.46%	115%
10000000 ng/ml	1850-1-2-2 R-3	10/31/2002	11414578			
Blank	1850-1-2 Blank 3	11/6/2002	252250 U			
10000000 ng/ml	1850-1-2-3 R-1	11/6/2002	11518386			
10000000 ng/ml	1850-1-2-3 R-2	11/6/2002	10995772	11202106	2.48%	112%
10000000 ng/ml	1850-1-2-3 R-3	11/6/2002	11092161			
Blank	1850-1-2 Blank 4	11/14/2002	252250 U			
10000000 ng/ml	1850-1-2-4 R-1	11/14/2002	11069468			
10000000 ng/ml	1850-1-2-4 R-2	11/14/2002	10948138	11168052	2.53%	112%
10000000 ng/ml	1850-1-2-4 R-3	11/14/2002	11486549			
Blank	1850-1-2 Blank 5	11/19/2002	252250 U			
10000000 ng/ml	1850-1-2-5 R-1	11/19/2002	10405755			
10000000 ng/ml	1850-1-2-5 R-2	11/19/2002	10625529	10501667	1.07%	105%
10000000 ng/ml	1850-1-2-5 R-3	11/19/2002	10473718			
Blank	1850-1-2 Blank 6	12/6/2002	252250 U			
10000000 ng/ml	1850-1-2-6 R-1	12/6/2002	10334737			
10000000 ng/ml	1850-1-2-6 R-2	12/6/2002	10469911	10545771	2.44%	105%
10000000 ng/ml	1850-1-2-6 R-3	12/6/2002	10832666			
Blank	1850-1-2 Blank 7	12/11/2002	252250 U			
10000000 ng/ml	1850-1-2-7 R-1	12/11/2002	9963159			
10000000 ng/ml	1850-1-2-7 R-2	12/11/2002	10391345	10219222	2.21%	102%
10000000 ng/ml	1850-1-2-7 R-3	12/11/2002	10303163			
Blank	1850-1-2 Blank 8	12/18/2002	252250 U			
10000000 ng/ml	1850-1-2-8 R-1	12/18/2002	10252964			
10000000 ng/ml	1850-1-2-8 R-2	12/18/2002	10266852	10292766	0.56%	103%
10000000 ng/ml	1850-1-2-8 R-3	12/18/2002	10358482			
Blank	1850-1-2 Blank 9	1/8/2003	252250 U			
10000000 ng/ml	1850-1-2-9 R-1	1/8/2003	10521219			
10000000 ng/ml	1850-1-2-9 R-2	1/8/2003	10340508	10189831	4.19%	102%
10000000 ng/ml	1850-1-2-9 R-3	1/8/2003	9707765			
Blank	1850-1-2 Blank 10	1/16/2003	252250 U			
10000000 ng/ml	1850-1-2-10 R-1	1/16/2003	10520070			
10000000 ng/ml	1850-1-2-10 R-2	1/16/2003	10839213	10677690	1.49%	107%
10000000 ng/ml	1850-1-2-10 R-3	1/16/2003	10673788			

[1] Recovery is relative to the target concentration

U = Not detected at a value greater than the MDL

Table C.2. CCV Data for Ketoconazole Concentration in Mazola Corn Oil

Date	Sample Name	Ketoconazole (ng/mL)	Recovery	PD
10/24/02	PP-1191C500ng/mlCCV	513	103%	2.67%
10/24/02	PP-1191C500ng/mlCCV	500	100%	0.08%
10/31/02	PP-1191C500ng/mlCCV	557	111%	11.4%
10/31/02	PP-1191C500ng/mlCCV	487	97.4%	2.62%
11/6/02	PP-1191C500ng/mlCCV	501	100%	0.20%
11/6/02	PP-1191C500ng/mlCCV	496	99.2%	0.78%
11/14/02	PP-1191C500ng/mlCCV	516	103%	3.28%
11/14/02	PP-1191C500ng/mlCCV	460	92.0%	8.02%
11/19/02	PP-1199C500ng/mlCCV	493	98.6%	1.39%
11/19/02	PP-1199C500ng/mlCCV	461	92.2%	7.83%
11/19/02	PP-1199C500ng/mlCCV	496	99.1%	0.87%
12/06/02	PP-1199C500ng/mlCCV	470	94.1%	5.94%
12/06/02	PP-1199C500ng/mlCCV	487	97.3%	2.65%
12/11/02	PP-1199C500ng/mlCCV	547	109%	9.33%
12/11/02	PP-1199C500ng/mlCCV	462	92.3%	7.68%
12/18/02	PP-1199C500ng/mlCCV	534	107%	6.78%
12/18/02	PP-1199C500ng/mlCCV	486	97.2%	2.84%
1/8/03	PP-1199C500ng/mlCCV	514	103%	2.70%
1/8/03	PP-1199C500ng/mlCCV	470	94.1%	5.94%
1/16/03	PP-1199C500ng/mlCCV	472	94.5%	5.53%
1/16/03	PP-1199C500ng/mlCCV	530	106%	6.02%

Table C.3. Internal Standards Data for Ketoconazole in Mazola Corn Oil

Sample Name	Date	5A Androstane Recovery
Not Applicable		

Table C.4. Peroxide concentration in Mazola Corn Oil (meq/kg)

Sample	Analysis Date	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	09/05/02	0.5	0.005	5.00	0.50		
Mazola Corn Oil Expiration 6-03 R-1	09/05/02	1.9	0.005	5.01	1.90		
Mazola Corn Oil Expiration 6-03 R-2	09/05/02	1.8	0.005	5.36	1.68	1.77	6.41
Mazola Corn Oil Expiration 6-03 R-3	09/05/02	1.8	0.005	5.16	1.74		
Mazola Corn Oil Expiration 1-04 R-1	09/05/02	1.2	0.005	4.92	1.22		
Mazola Corn Oil Expiration 1-04 R-2	09/05/02	1.5	0.005	5.2	1.44	1.34	8.31
Mazola Corn Oil Expiration 1-04 R-3	09/05/02	1.4	0.005	5.13	1.36		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-02
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

———— 5/31/2003 8:08:10 AM ————————————————————

Results for: Week 0

1 = bottom
2 = top

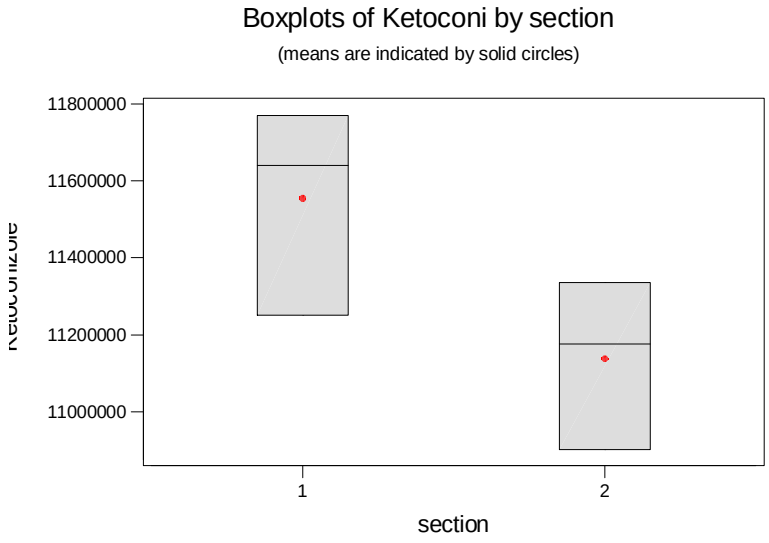
Two-Sample T-Test and CI: Ketoconazole, section

```
Two-sample T for Ketoconazole
section     N      Mean     StDev   SE Mean
1           3  11554197    269649    155682
2           3  11138266    219807    126905

Difference = mu (1) - mu (2)
Estimate for difference:  415931
95% CI for difference: (-223273, 1055135)
T-Test of difference = 0 (vs not =): T-Value = 2.07  P-Value = 0.130  DF = 3
```

Very poor power!

NS



Kruskal-Wallis Test: Ketoconazole versus section

```
Kruskal-Wallis Test on Ketoconazole

section     N    Median    Ave Rank         Z
1           3  11641456         4.7      1.53
2           3  11177361         2.3     -1.53
Overall     6                   3.5

H = 2.33  DF = 1  P = 0.127

* NOTE * One or more small samples
```

Conclusion: For the week 0 data, the test between sections has very poor power, note the width of the 95% CI of the difference (-223273, 1055135). Because one sample from both the top and bottom sections was about the same concentration, no difference could be detected.

Results for: Stability Data

- Performs a one-sample t-test for mu less than TARGET &

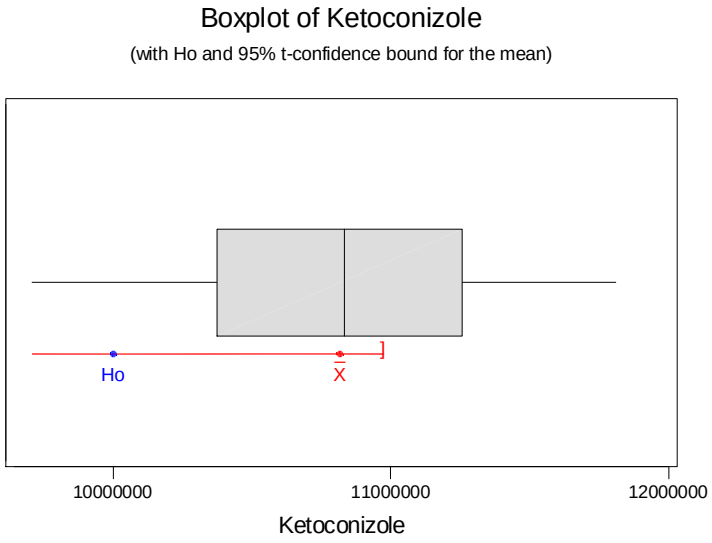
```
What is the target value for X    3
DATA> 10000000
```

One-Sample T: Ketoconazole

```
Test of mu = 10000000 vs mu < 10000000

Variable          N      Mean     StDev   SE Mean
Ketoconazole     33  10816801    535803     93271

Variable      95.0% Upper Bound        T      P
Ketoconazole           10974792     8.76  1.000      NS
```



- Outliers are < Median-3*IQD OR > Median+3*IQD

```
Boundary for outliers are values <     8186855  and >     13478477

No outliers
```

- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	16.2294
0	2	16.2435
0	3	16.2044
0	1	16.2701
0	2	16.2810
0	3	16.2360
1	1	16.2369
1	2	16.2844
1	3	16.2504
2	1	16.2595
2	2	16.2130
2	3	16.2217
3	1	16.2197
3	2	16.2087
3	3	16.2567
4	1	16.1579
4	2	16.1788
4	3	16.1644
6	1	16.1510
6	2	16.1640
6	3	16.1981
7	1	16.1144
7	2	16.1565
7	3	16.1480
8	1	16.1431
8	2	16.1444
8	3	16.1533
11	1	16.1689
11	2	16.1516
11	3	16.0884
12	1	16.1688
12	2	16.1987
12	3	16.1833

- Conducts Simple Linear Regression

Regression Analysis: Ketoconazole versus Week

The regression equation is
Ketoconazole = 16.2 - 0.00893 Week

Predictor	Coef	SE Coef	T	P	
Constant	16.2393	0.0093	1748.65	0.000	
Week	-0.008933	0.001462	-6.11	0.000	**

S = 0.03386 R-Sq = 54.6% R-Sq(adj) = 53.2%

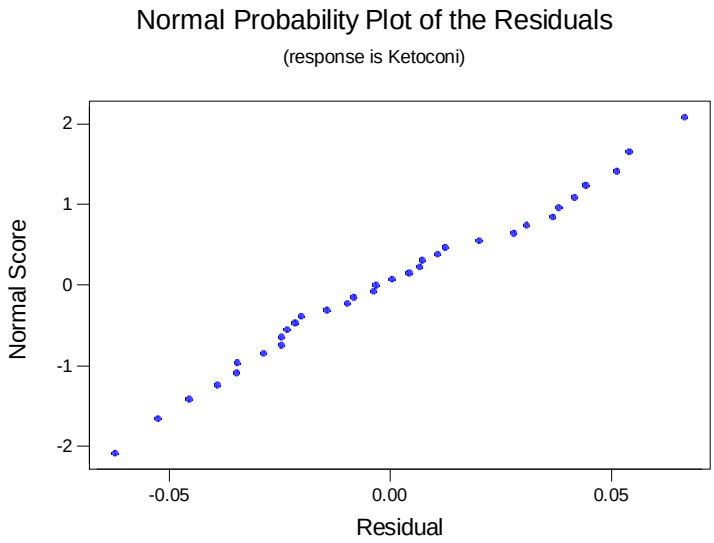
Analysis of Variance

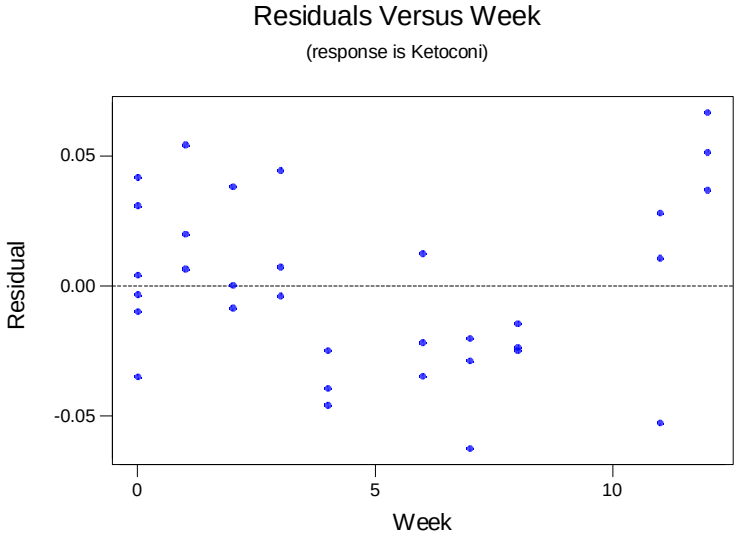
Source	DF	SS	MS	F	P	
Regression	1	0.042826	0.042826	37.34	0.000	
Residual Error	31	0.035551	0.001147			
Lack of Fit	8	0.021483	0.002685	4.39	0.002	**
Pure Error	23	0.014068	0.000612			
Total	32	0.078377				

Unusual Observations

Obs	Week	Ketoconazole	Fit	SE Fit	Residual	St Resid
32	12.0	16.1987	16.1321	0.0119	0.0666	2.10R

```
R denotes an observation with a large standardized residual
```






```
Do you want to remove any data points? (yes OR no)
n

Should a quadratic be fit? (yes OR no)
n
```

- Power analysis for t-test of slope less than zero

Power and Sample Size

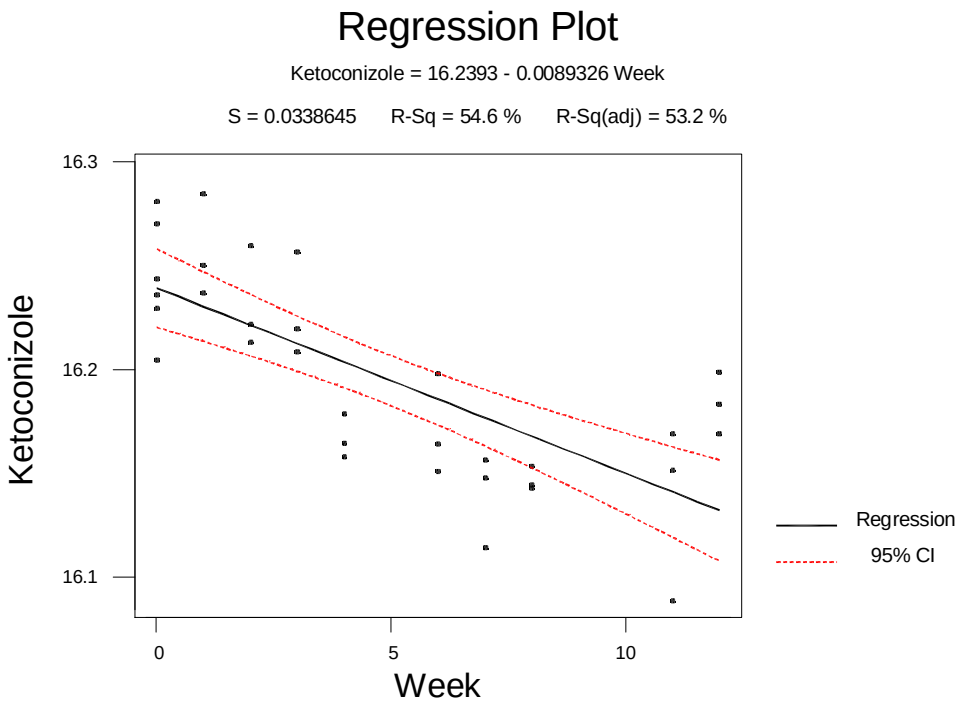
```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0338645

Sample
  Size   Power  Difference
    31  0.9900     -0.0247
```

- That means we would detect a mean of 16.093 as significantly less than ln(10000000) = 16.118 or a change of 9756025 from 10000000 = 2.4% loss.

- Fit 95% confidence bands about the fitted simple linear model



- Evaluate stability using the average Day 0 concentration as the target

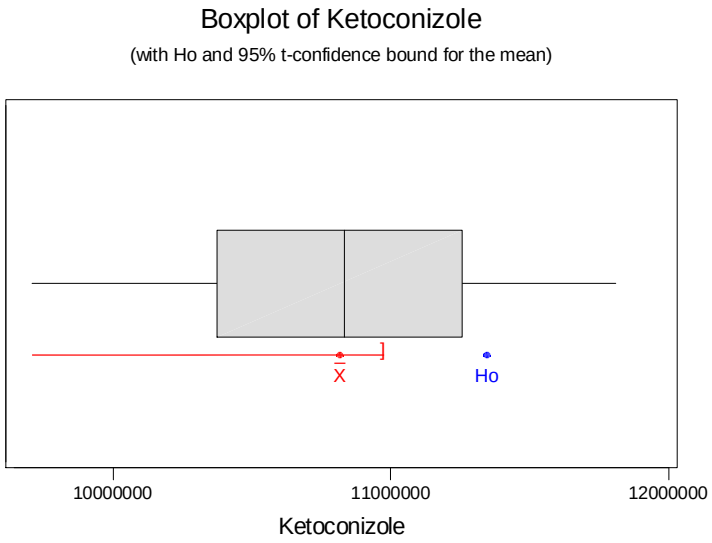
One-Sample T: Ketoconazole

```
Test of mu = 11346232 vs mu < 11346232

Variable          N      Mean     StDev   SE Mean
Ketoconazole     33  10816801    535803     93271

Variable      95.0% Upper Bound        T      P
Ketoconazole           10974792    -5.68  0.000      **
```

t Boxplot of Ketoconazole



- **Conclusion – all but two data points were greater than the target concentration of 10,000,000 mg/L, thus stability was evaluated using the average Day 0 concentration. The slope through time was significant and the concentration was expected to stay above 90% of the Day 0 concentration for only 8 weeks. Thus, the chemical is stable for only 8 weeks.**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Ketoconazole in-life test suspension samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Ketoconazole suspended in corn oil

TEST SOLUTION, SAMPLE CUSTODY, AND PROCESSING:

Test suspensions of ketoconazole (CAS 65277-42-1) supporting EDSP WA 2-14 were made on 11/20/02 (females) and 01/22/03 (males) at two test concentrations (10 mg/mL and 20 mg/mL) for female and male rat exposures. The 10 mg/mL concentration was prepared by weighing 2.0 g of ketoconazole (CF 1850, Spectrum Lot # QL0352, expiration date 09/05) into a 250 mL, wide-mouth, amber glass bottle and adding 184 g Mazola corn oil. The 20 mg/mL concentration was prepared by weighing 4.0 g ketoconazole and adding 182 g Mazola corn oil (corn oil was from containers with the following expiration dates: 6/12/03, 1/1/04, and 4/24/04).

The test suspension was sampled four times during the female test (11/27/02, 12/03/02, 12/10/02, and 12/17/02) and five times during the male test (01/26/03, 02/02/03, 02/09/03, 02/16/03, and 02/23/03). Data are reported in Table 3 for males and Table 4 for females. Table 5 provides results of analysis of remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test.

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:

The samples were stirred and stored in a refrigerator. Samples for female rat exposures were collected to verify test concentrations on 11/20/02 and analyzed on 11/21/02. Replicate 1 samples were shipped on 11/21/02 and Replicate 2 on 11/25/02. Samples for male rat exposures were collected to verify test concentrations on 01/23/03 and analyzed on 01/24/03. Replicate 1 samples were shipped on 01/23/03 and Replicates 2 and 3 on 01/27/03.

Test-suspension samples analyzed to verify test concentrations were stirred and 1 mL sampled from the middle of the container and transferred to a 60 mL, tared, amber glass bottle. Sample weight was determined gravimetrically. 50 mL acetonitrile (ACN, JT Baker lot # 448346) was added and the container agitated. Then, 0.01 mL (10 mg/mL concentration) or 0.995 mL (20 mg/mL concentration) was transferred to an auto sampler vial with either 0.99 mL or 0.005 mL, respectively, of 60% ACN in water. This solution was analyzed on the high-performance liquid chromatograph (HPLC) using an ultraviolet/visible (UV/VIS) detector at the 245 nm wavelength. A 70:30% ACN:water (v:v) buffer was used as an eluent at 1.5 mL/min. The eluent was made by adding 75 mL buffer (50 mM phosphate with pH adjusted to 7 with sodium hydroxide [NaOH]), 75 mL deionized water and 350 mL ACN. Separation was attained using a Supelco petroleum aromatic hydrocarbon (PAH) column (a C-18

column). Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1199, A-E.

In-life and Returned Container Samples:

Samples were returned from RTI at two different times, on 12/18/02 for female rat assays (received at Battelle, Sequim, WA, on 12/20/02) and on 03/04/03 for male rat assays (received at Battelle, Sequim, WA, on 03/05/03). Containers with remaining test solution from Replicate 2 samples were returned in 250 mL, amber glass bottles. In-life females exposure samples returned in 20 mL, scintillation vials contained about 5 mL of solution that was a slurry with much of the ketoconazole settled to the bottom of the vial, so the whole sample was extracted.

In-life samples were removed from the refrigerator and allowed to warm to ambient room temperature. Samples of remaining dosing solution were stirred overnight. On 01/16/03, a 0.5 or 1.0 mL subsample from the remaining containers was collected from the middle of the solution and placed in a tared, 60 mL, amber glass bottle. At this time, the sample weight was determined gravimetrically.

For the 20 mL scintillation vials, the vial was weighed, and the contents poured into a 60 mL, amber-glass bottle. Part of the 50 mL ACN was used to rinse the vial 3 times, and the amber bottles were agitated to mix. The vials were cleaned and dried using methylene chloride (MeCl) (JT Baker, lot# 36E04), air dried, and re-weighed. The sample volume is the difference between the initial sample plus the vial weight, minus the empty vial weight.

For the remaining samples, 50 mL ACN (JT Baker lot # 448346) was added and the container agitated. Then, 0.01 mL was transferred to an auto sampler vial with 0.99 mL 70:30% ACN:water (v:v) buffer. This solution was analyzed on the HPLC using a UV/VIS detector at the 245 nm wavelength. A 70:30% ACN:water (v: v) buffer was used as an eluent at 1.5 mL/min. The eluent was made by adding 75 mL buffer (50 mM phosphate with pH adjusted to 7 with NaOH), 75 mL DI water and 350 mL ACN or the equivalent in proportion. Separation was attained using a Supelco PAH column (a C-18 column). Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1199, A-E. Calibrations from data collected on 10/24/02, 11/19/02 and 12/06/02 were used, although calibration sets were analyzed with each batch of samples. Blanks were run with each sample batch and an initial calibration verification (ICV) sample and a continuing calibration verification (CCV) sample analyzed with each sample set analyzed. HPLC-run data are stored on computer WV04738. A multiplier of 5000 is used in the STAR software (50 mL ACN/ 0.01 mL sample). A corn oil blank is analyzed with the samples.

SAMPLE ANALYSIS The samples were analyzed by a modified SW 846 method, 8316, using an HPLC with a UV/VIS detector at the 245 nm wavelength.

Data Quality Objectives	Control Limits
Procedural Blank	<5 X MDL
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: Modified SW 846 method, 8316, using an HPLC with a UV/VIS detector at the 245 nm wavelength.

CALIBRATION: Calibration with a five-point curve was conducted using dilutions prepared from the calibration standard PP-1199, A-E, and a blank and a CCV sample were analyzed at the beginning and end of every run. Calibrations from 11/19/02 were used with the 11/21/02 run, and the calibration from 12/06/02 was used with the 01/16/03, 01/24/03, and 05/28/03 runs.

CONTINUING STANDARD RECOVERY: Percent recovery results for the nine initial and CCV samples analyzed with the in-life sample data set ranged from 90% to 108%, with a mean recovery of 99%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK Ketoconazole was not detected above the detection limit in the five blanks analyzed with the test solution and in-life samples.

DETECTION LIMIT: The ketoconazole detection limit was 252 mg/L, as determined by an MDL study using the low calibration standard (50.45 mg/L) reported with the data. No data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed.

REPLICATE ANALYSIS: The percent relative standard deviation (% RSD) for the two test solutions prepared for the ketoconazole female test range from 2.18 to 3.09.

The % RSD for the two ketoconazole male test solutions ranged from 0.518 to 2.29.

Replicate samples were not submitted for the in-life sample sets.

Table 1. Verification of Ketoconazole Female Test Solution Concentrations Prepared on 11/20/2002 and Analyzed on 11/21/02

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	%RSD
	WA 2-14 Y,Z Blank	0.252 U		
10 mg/mL	WA 2-14-Y-F Rep1 R1	9.84		
10 mg/mL	WA 2-14-Y-F Rep1 R2	9.80	10.0	3.09
10 mg/mL	WA 2-14-Y-F Rep1 R3	10.4		
20 mg/mL	WA 2-14-Z-F Rep1 R1	17.9		
20 mg/mL	WA 2-14-Z-F Rep1 R2	18.5	18.4	2.18
20 mg/mL	WA 2-14-Z-F Rep1 R3	18.7		

Table 2. Verification of Ketoconazole Male Test Solution Concentrations Prepared on 1/22/03 and Analyzed on 1/24/03

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	%RSD
	Sent to RTI Blank1	0.252 U		
10 mg/mL	2-14 F-M rep1	10.3		
10 mg/mL	2-14 F-M rep2	10.7	10.6	2.29
10 mg/mL	2-14 F-M rep3	10.7		
20 mg/mL	2-14 G-M rep1	21.6		
20 mg/mL	2-14 G-M rep2	21.7	21.6	0.518
20 mg/mL	2-14 G-M rep3	21.5		

Table 3. In-life Sample Ketoconazole Concentrations - Males

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
01/26/03	03/05/03	05/23/03	10 mg/mL	1-26 F-M	8.46	85%
02/02/03	03/05/03	05/23/03	10.mg/mL	2-2 F-M	8.59	86%
02/09/03	03/05/03	05/23/03	10 mg/mL	2-9 F-M	9.98	100%
02/16/03	03/05/03	05/23/03	10 mg/mL	2-16 F-M	10.1	101%
02/23/03	03/05/03	05/23/03	10 mg/mL	2-23 F-M	10.2	102%
01/26/03	03/05/03	05/23/03	20 mg/mL	1-26 G-M	18.8	94%
02/02/03	03/05/03	05/23/03	20 mg/mL	2-2 G-M	19.8	99%
02/09/03	03/05/03	05/23/03	20 mg/mL	2-9 G-M	19.8	99%
02/16/03	03/05/03	05/23/03	20 mg/mL	2-16 G-M	19.1	96%
02/23/03	03/05/03	05/23/03	20 mg/mL	2-23 G-M	18.2	91%

Table 4. In-life Sample Ketoconazole Concentrations – Females

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
11/27/02	12/20/02	01/16/03	10 mg/mL	2-14-Y-F 11-27-02	8.09	81%
12/03/02	12/20/02	01/16/03	10.mg/mL	2-14-Y-F 12-03-02	10.8	108%
12/10/02	12/20/02	01/16/03	10 mg/mL	2-14-Y-F 12-10-02	10.9	109%
12/17/02	12/20/02	01/16/03	10 mg/mL	2-14-Y-F 12-17-02	8.37	84%
11/27/02	12/20/02	01/16/03	20 mg/mL	2-14-Z-F 11-27-02	19.2	96%
12/03/02	12/20/02	01/16/03	20 mg/mL	2-14-Z-F 12-03-02	19.4	97%
12/10/02	12/20/02	01/16/03	20 mg/mL	2-14-Z-F 12-10-02	20.5	103%
12/17/02	12/20/02	01/16/03	20 mg/mL	2-14-Z-F 12-17-02	11.6	58%

Table 5. Ketoconazole Post-Test Concentrations in Formulation Samples Returned to Battelle from RTI

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
11/20/02	12/20/02	01/16/03	10 mg/mL	2-14-y-f R-2, remainder	11.2	112%
01/22/03	03/05/03	05/28/03	10 mg/mL	Remain2-14 F-M rep3	10.1	101%
11/20/02	12/20/02	01/16/03	20 mg/mL	2-14-z-f R-2, remainder	21.9	110%
01/22/03	03/05/03	05/28/03	20 mg/mL	Remain2-14 G-M rep3	20.0	100%

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Linuron in Mazola Corn Oil

November 3, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory

1529 West Sequim Bay Road

Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology

Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Linuron in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Linuron in Mazola Corn Oil

Parameter	Chemical
Compound Name	Linuron
CAS #	330-55-2
Central File No.	CF-1824
Initial Receipt Date	9/3/2002
Expiration Date	11/05
Manufacturer	ChemService, Inc.
Lot Number	273-81B
Battelle Study #	WA 2-14-02-02
Method	SW 846, 8316 Modified

Executive Summary

The chemical purity of linuron determined by the manufacturer was 99%. The purity analysis by Battelle Sequim using HPLC showed it to be 99.5% pure. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of linuron was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 15 weeks. Thus, stability testing of the linuron stock solution in corn oil was considered stable at the 10 mg/mL concentration for the required testing and holding period of 12 weeks.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on the target concentration ranged from 95% to 123%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA 2-14-02-02, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of linuron (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_Linuron-cornoil.doc, PSTP_WA-2-14_Linuron-cornoil.doc, DSUM_WA2-14_Linuron-crnoil.xls, and DAF_WA-2-14_Linuron-cornoil.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, linuron, (CAS No. 330-55-2) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Linuron was purchased from ChemService, Inc., and lot number 273-81B was initially received on 9/3/2002 with an expiration date of 11/05 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1824) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-02

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Linuron (MSL CF 1824)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 10 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Testing/holding duration: 12 weeks

Chemical Information

Chemical Name: Linuron

CAS: 330-55-2

Any known purity information: may refer to attached documentation	Manufacturer's Purity Information: 99% pure
Any known stability information: may refer to attached documentation	None available
Desired purity (%) for test? 95% or greater	

Figure 1. EDSP Requisition Form for Linuron

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Linuron
CAS #	330-55-2
Central File No.	CF-1824
Initial Receipt Date	9/3/2002
Expiration Date	11/05
Manufacturer	ChemService, Inc.
Lot Number	273-81B
Manufacturer's Purity	99%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA 2-14-02-02
Method	SW 846, 8316 Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted on a high performance liquid chromatograph (HPLC) with ultraviolet (UV) absorbance at 250 nm by taking a solution of about 5000 ng/mL in 60% acetonitrile (ACN): 40% de-ionized water solution. This matrix was then run on the HPLC and the purity determined by comparing the peak heights of the peaks in the chromatogram. The purity was determined by first identifying the peaks in the chromatogram of the linuron that were the same as the peaks in the analysis of the blank sample. The areas associated with these common peaks were then eliminated by inhibiting integration and the remaining peaks were reported as a percentage of the total peak area. The percentage associated with the largest peak represented the purity of linuron. The HPLC was set up with an auto sampler and a column oven. The column oven temperature was set at 30ºC, and the auto sampler was set to inject 250 µL of the matrix. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. A stock solution was prepared to arrive at the chemical concentration requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

A linuron stock matrix was prepared on 10/24/02 for testing as described in Table 2. Briefly, for the 10 mg/mL linuron, 2.0 g of linuron were weighed into a 250 mL wide-mouth amber glass bottle and 184 g of Mazola corn oil were added to obtain the desired concentration. A stir bar was added, and the mixture was agitated on a stir plate. All solutions were transferred to ashed, amber bottles. Bottles were labeled and stored at 4ºC ± 2ºC for the duration of the test.

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA 2-14-02-02 12 Weeks	Linuron	10 mg/mL	1824-2a-2	2.0 g Linuron in 184 g Mazola corn oil

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by chromatographic analysis. Triplicate aliquots were tested for the 10 mg/mL concentration. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

Stability testing of linuron was performed by removing the stock from the refrigerator, allowing it to warm to room temperature, and then removing triplicate 1 mL samples from the middle of the container. Each sample was placed in a tared 60 mL amber bottle, and the sample weight was determined gravimetrically. Next, 50 mL of ACN (JT Baker lot # 44836) were added and the container was agitated. Then, 0.01 mL was transferred to an auto sampler vial with 0.99 mL 60% ACN in water. This solution was analyzed on the HPLC using a UV/VIS detector at the 250 nm wavelength. A 60:40% ACN:water buffer was used as an effluent at 1.5 mL/min. Separation was attained using a Supelco PAH column (a C-18 column). Calibration was done using dilutions prepared from standard PP-1192 with a 5-point standard curve. HPLC run data were stored on computer WV04738. A multiplier of 5000 was used in the STAR software (50 mL ACN/ 0.01 mL sample). A corn oil blank was analyzed with the samples.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a HPLC purity scan on the linuron. Standard PP-1192A at 5000 ng/ml was run and compared to the blank. The area of the linuron peak was then compared to all the peaks in the chromatogram which have had the blank peak areas subtracted and a percent purity was determined by the percent the linuron peak contributed to the total peak area. The area of the linuron peak was 99.5% of the total area of all peaks in the chromatogram. Chemical purity of linuron determined by the manufacturer was 99% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 10/25/02. Chemical concentration was determined 10 times between 10/25/02 and 01/17/03. The analytical and quality control (QC) results are presented in Appendix C. A single preparation blank was analyzed with every batch for quality control purposes. There were no detectable concentrations of linuron in the blanks. Continuing calibration verification (CCV) results ranged from 92.5% to 103%. Internal standards were not analyzed. The MDL was 247,900 ng/mL. The dilution factor of the formulation can be taken into account, and thus, the MDL of the diluted sample was 49.6 ng/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg as required for biological testing (Appendix C). The average peroxide number in the Mazola corn oil was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide is consistent with the request that the oil have a peroxide number less than 3 meq/kg.

3.3 Statistical Results of Stability Trial

A plot of linuron with a target concentration of 10,000,000 ng/mL against time shows that all but one observation was greater than the target concentration (Figure 2). Therefore, the average day 0 concentration was tested for stability. Only one data point was less than 90% of the average day 0 concentration. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of linuron was expected to stay greater than or equal to 90% of the average day 0 concentration for up to an estimated 15 weeks (Table 3). Thus, this stock solution was considered stable for the required 12-week testing/holding period. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses based on target concentrations ranged from 95% to 123%. The complete analysis is presented in Appendix E.

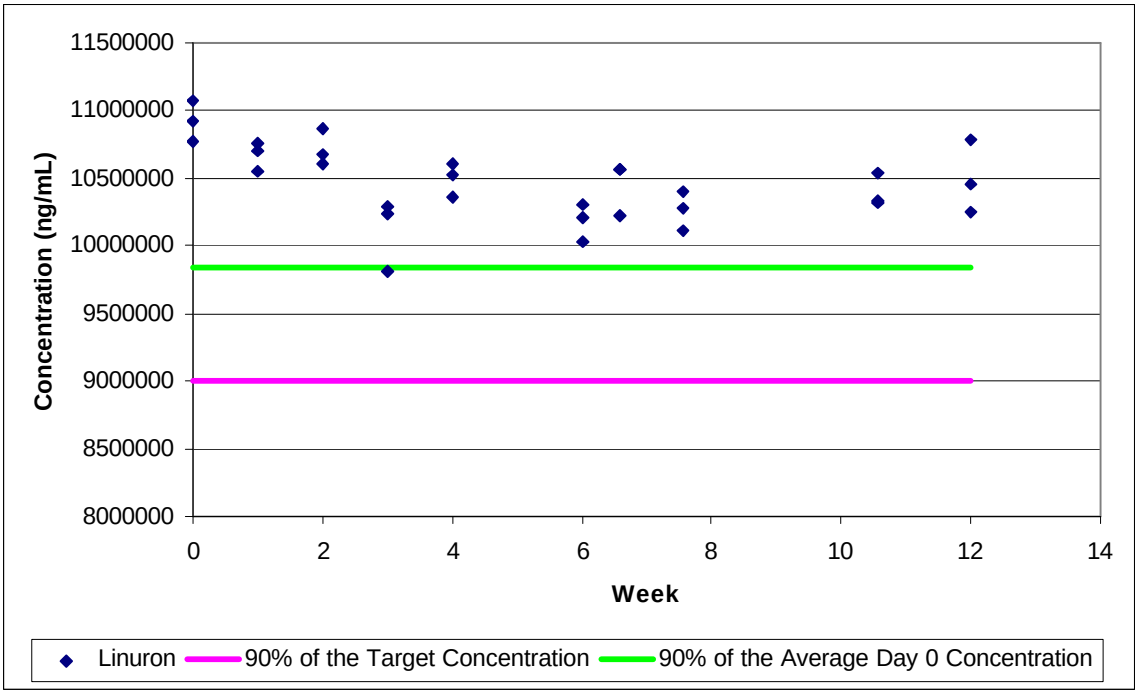


Figure 2. Observed Concentration of Linuron with a Target Concentration of 10,000,000 ng/mL Against Time

Table 3. Summary of Statistical Results for Linuron

Statistical Analysis conducted by Valerie Cullinan Using Minitab Version 13.32, Minitab Inc., 1999.	WA-2-14-02-02 1824-2a-2 Linuron
Average Day 0 Concentration (ng/mL)	10925553
Number of determinations	1
Number of weeks tested	12
Number of replicates per day	3
Number of outliers removed	0
Number of observations removed	0
Overall Mean Concentration	10472557
95% Upper CL	10559845
error degrees of freedom	29
1-sample t-test of Ho: μ >= Target	S [a]
estimated intercept of ln(concentration) against time	16.1783
estimated slope of ln(concentration) against time	-0.0027
standard error of slope	0.0012
error degrees of freedom	28
Significance test of lack-of-fit for final model	S
Significance test of Ho: b = 0 vs. H1: b ? 0	S
Lower 95% CL	-0.005
Upper 95% CL	0.000
Maximum Percent Loss (using LCL)	4.0%
Mean Percent Loss (using bhat)	2.1%
LN(90% of Target)	16.1013
Number of weeks until at 90% of Target (using LCL)	15
Conclusion:	**Stable for 12 wks**

[a]Significant at a = 0.05

4.0 CONCLUSIONS

According to the manufacturer, the purity of linuron was 99%; Battelle-Sequim determined linuron purity to be 99.5%. Stability testing of linuron in Mazola corn oil concluded that the chemical was stable at the 10 mg/mL concentration for a period of 12 weeks.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 95% to 123%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

Chem Service INC
660 Tower Lane • P.O. Box 599 • West Chester, PA 19381-0599
1-800-452-9994 • 1-610-692-3026 • Fax 1-610-692-8729
info@chemservice.com • www.chemservice.com

CERTIFICATE OF ANALYSIS

INVOICE #: CS237091
PO #: 11180291EAC

CATALOG #: PS-372 CAS #: 330-55-2

DESCRIPTION: Linuron

LOT #: 273-81B

PURITY: 99%

EXPIRATION DATE: 11/05

Chem Service, Inc. guarantees the purity of this chemical ± 0.5% deviation prior to the expiration date shown on the label and exclusive of any customer contamination.

Two or more of the following methods of analysis are used to determine purity: Melting point, refractive index, titration, FTIR, IR, TLC, GC/FID, GC/TCD, GC/ECD, GC/MS, HPLC or DSC.

Our standards are suitable for use with all EPA methods.

Certified By:

John Conrad

John Conrad
CSM/TC

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Linuron

Chemical Name: Linuron (MSL CF 1824)

CAS Number: 330-55-2

Lot Number: 273-81B stored at RT in MSL5, Rm 219

Expiration date: 11/05

Manufacturer's Purity Information: 99%

Manufacturer's Stability Information: none

MSL Purity Results:
Purity (%) To be determined at MSL by LC

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Linuron

CAS: 330-55-2

Carrier(s): Mazola corn oil

Concentrations/Dilution Series: 10mg/mL

In vitro or in *vivo tests*? *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Testing/holding duration: 12 weeks

Design of Stability Test: 10 mg/mL in glass at 4 deg. C in the dark for 12 weeks, analyzed at least 8 times in triplicate

Number of replicates: 3

Duration: 12 weeks

Other factors:

Temperature regime(s): 4 deg. C

Test container type: glass

Light or dark: dark except when container is removed for sampling or handling

Other

Statistical testing: regression analysis of the slope for concentration versus time

Resulting records package:

Manufacturer's certificate of analysis or purity

MSDS

Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
  - Chemical repository confirmatory test results of chemical identity and purity;
  - Chemical repository test results of lot-to-lot variation in chemical purity;
  - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- Dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. Linuron Concentration in Mazola Corn Oil (ng/mL)

Target Concentration	Sample Name	Date	Linuron	Average	RSD	Recovery[1]
Blank	1824-2a-2 Blank 1	10/25/2002	247900 U			
10000000 ng/ml	1824-2a-2-1 R-1	10/25/2002	10919504			
10000000 ng/ml	1824-2a-2-1 R-2	10/25/2002	11081135	10925553	1.40%	109%
10000000 ng/ml	1824-2a-2-1 R-3	10/25/2002	10776021			
Blank	1824-2a-2 Blank 2	11/1/2002	247900 U			
10000000 ng/ml	1824-2a-2-2 R-1	11/1/2002	10700503			
10000000 ng/ml	1824-2a-2-2 R-2	11/1/2002	10752458	10670332	0.94%	107%
10000000 ng/ml	1824-2a-2-2 R-3	11/1/2002	10558034			
Blank	1824-2a-2 Blank 3	11/8/2002	247900 U			
10000000 ng/ml	1824-2a-2-3 R-1	11/8/2002	10674884			
10000000 ng/ml	1824-2a-2-3 R-2	11/8/2002	10868587	10715381	1.28%	107%
10000000 ng/ml	1824-2a-2-3 R-3	11/8/2002	10602671			
Blank	1824-2a-2 Blank 4	11/15/2002	247900 U			
10000000 ng/ml	1824-2a-2-4 R-1	11/15/2002	10291960			
10000000 ng/ml	1824-2a-2-4 R-2	11/15/2002	9812076	10115202	2.61%	101%
10000000 ng/ml	1824-2a-2-4 R-3	11/15/2002	10241571			
Blank	1824-2a-2 Blank 5	11/22/2002	247900 U			
10000000 ng/ml	1824-2a-2-5 R-1	11/22/2002	10365415			
10000000 ng/ml	1824-2a-2-5 R-2	11/22/2002	10601550	10498879	1.15%	105%
10000000 ng/ml	1824-2a-2-5 R-3	11/22/2002	10529671			
Blank	1824-2a-2 Blank 6	12/6/2002	247900 U			
10000000 ng/ml	1824-2a-2-6 R-1	12/6/2002	10036127			
10000000 ng/ml	1824-2a-2-6 R-2	12/6/2002	10216465	10187538	1.37%	102%
10000000 ng/ml	1824-2a-2-6 R-3	12/6/2002	10310022			
Blank	1824-2a-2 Blank 7	12/10/2002	247900 U			
10000000 ng/ml	1824-2a-2-7 R-1	12/10/2002	10227916			
10000000 ng/ml	1824-2a-2-7 R-2	12/10/2002	10572080	10455898	1.89%	105%
10000000 ng/ml	1824-2a-2-7 R-3	12/10/2002	10567697			
Blank	1824-2a-2 Blank 8	12/17/2002	247900 U			
10000000 ng/ml	1824-2a-2-8 R-1	12/17/2002	10399085			
10000000 ng/ml	1824-2a-2-8 R-2	12/17/2002	10112981	10262147	1.40%	103%
10000000 ng/ml	1824-2a-2-8 R-3	12/17/2002	10274375			
Blank	1824-2a-2 Blank 9	1/7/2003	247900 U			
10000000 ng/ml	1824-2a-2-9 R-1	1/7/2003	10329196			
10000000 ng/ml	1824-2a-2-9 R-2	1/7/2003	10319294	10396262	1.20%	104%
10000000 ng/ml	1824-2a-2-9 R-3	1/7/2003	10540296			
Blank	1824-2a-2 Blank 10	1/17/2003	247900 U			
10000000 ng/ml	1824-2a-2-10 R-1	1/17/2003	10252507			
10000000 ng/ml	1824-2a-2-10 R-2	1/17/2003	10781512	10498379	2.54%	105%
10000000 ng/ml	1824-2a-2-10 R-3	1/17/2003	10461118			

[1] Recovery is relative to the target concentration

U = Not detected at a value greater than the MDL

Table C.2. CCV Data for Linuron Concentration in Mazola Corn Oil

Sample Name	Linuron (ng/ml)	Recovery	PD
PP-1192C500ng/mlCCV	483	96.6%	3.38%
PP-1192C500ng/mlCCV	489	97.8%	2.19%
PP-1192C500ng/mlCCV	486	97.2%	2.85%
PP-1192C500ng/mlCCV	489	97.8%	2.24%
PP-1192C500ng/mlCCV	509	102%	1.82%
PP-1192C500ng/mlCCV	517	103%	3.47%
PP-1192C500ng/mlCCV	466	93.2%	6.83%
PP-1192C500ng/mlCCV	462	92.5%	7.52%
PP-1192C500ng/mlCCV	482	96.3%	3.70%
PP-1192C500ng/mlCCV	479	95.7%	4.28%
PP-1192C500ng/mlCCV	474	94.8%	5.23%
PP-1192C500ng/mlCCV	472	94.5%	5.54%
PP-1192C500ng/mlCCV	479	95.8%	4.15%
PP-1192C500ng/mlCCV	476	95.2%	4.78%
PP-1192C500ng/mlCCV	477	95.3%	4.68%
PP-1192C500ng/mlCCV	480	95.9%	4.07%
PP-1192C500ng/mlCCV	495	98.9%	1.05%
PP-1192C500ng/mlCCV	492	98.4%	1.65%
PP-1192C500ng/mlCCV	495	99.0%	0.98%
PP-1192C500ng/mlCCV	490	98.0%	1.98%
PP-1192C500ng/mlCCV	494	98.8%	1.16%

Table C.3. Internal Standards Data for Linuron in Mazola Corn Oil

Sample Name	Date	Recovery

Not applicable

Table C.4. Peroxide Concentration in Mazola Corn Oil (meq/kg)

Sample	Analysis Date	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	09/05/02	0.5	0.005	5.00	0.50		
Mazola Corn Oil Expiration 6-03 R-1	09/05/02	1.9	0.005	5.01	1.90		
Mazola Corn Oil Expiration 6-03 R-2	09/05/02	1.8	0.005	5.36	1.68	1.77	6.41
Mazola Corn Oil Expiration 6-03 R-3	09/05/02	1.8	0.005	5.16	1.74		
Mazola Corn Oil Expiration 1-04 R-1	09/05/02	1.2	0.005	4.92	1.22		
Mazola Corn Oil Expiration 1-04 R-2	09/05/02	1.5	0.005	5.2	1.44	1.34	8.31
Mazola Corn Oil Expiration 1-04 R-3	09/05/02	1.4	0.005	5.13	1.36		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-02
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.
6/3/2003 1:05:25 PM

- Performs a one-sample t-test for mu less than 10,000,000

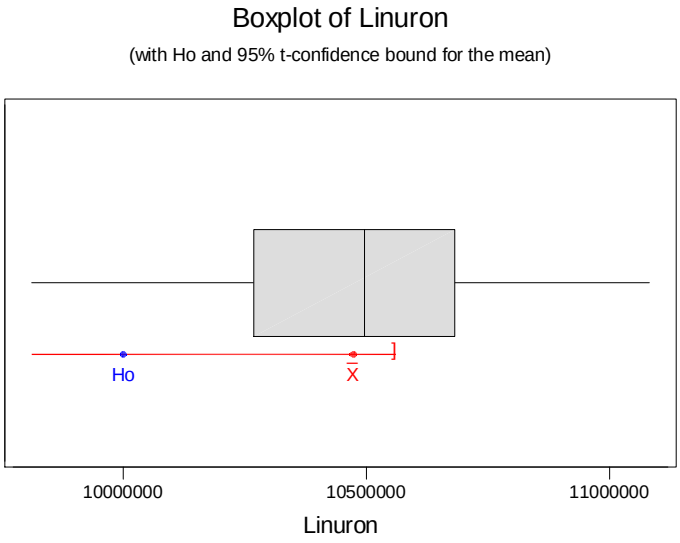
One-Sample T: Linuron

```
Test of mu = 10000000 vs mu < 10000000

Variable          N      Mean     StDev   SE Mean
Linuron          30  10472557    281376     51372

Variable      95.0% Upper Bound        T      P
Linuron                10559845     9.20  1.000
```

t Boxplot of Linuron



- All but one observation is less than the target concentration of 10,000,000 ng/mL. Therefore, test the average day 0 concentration for stability.

- Performs a one-sample t-test for mu less than the average day 0 concentration

```
What is the target value for X    3
DATA> 10925553
```

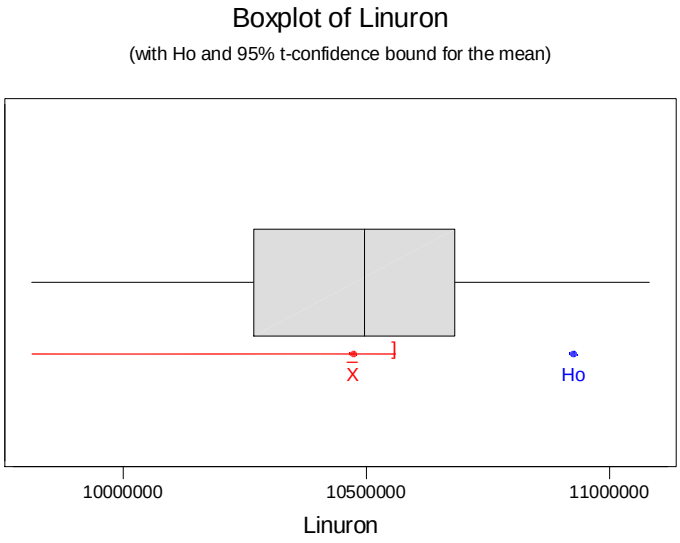
One-Sample T: Linuron

```
Test of mu = 10925553 vs mu < 10925553

Variable          N      Mean     StDev   SE Mean
Linuron          30  10472557    281376     51372

Variable      95.0% Upper Bound        T      P
Linuron                10559845    -8.82  0.000      **
```

t Boxplot of Linuron




```
Outliers are < Median-3*IQD OR > Median+3*IQD

Boundary for outliers are values <     9258252  and >     11732537

No outliers
```

- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	16.2061
0	2	16.2208
0	3	16.1928
1	1	16.1858
1	2	16.1906
1	3	16.1724
2	1	16.1834
2	2	16.2014
2	3	16.1766
3	1	16.1469
3	2	16.0991
3	3	16.1420
4	1	16.1540
4	2	16.1765
4	3	16.1697
6	1	16.1217
6	2	16.1395
6	3	16.1486
7	1	16.1406
7	2	16.1737
7	3	16.1733
8	1	16.1572
8	2	16.1293
8	3	16.1452
11	1	16.1505
11	2	16.1495
11	3	16.1707
12	1	16.1430
12	2	16.1933
12	3	16.1632

- Conducts Simple Linear Regression

Regression Analysis: Linuron versus Week

The regression equation is
Linuron = 16.2 - 0.00267 Week

Predictor	Coef	SE Coef	T	P	
Constant	16.1783	0.0078	2063.15	0.000	
Week	-0.002667	0.001177	-2.27	0.031	*

S = 0.02516 R-Sq = 15.5% R-Sq(adj) = 12.5%

Analysis of Variance

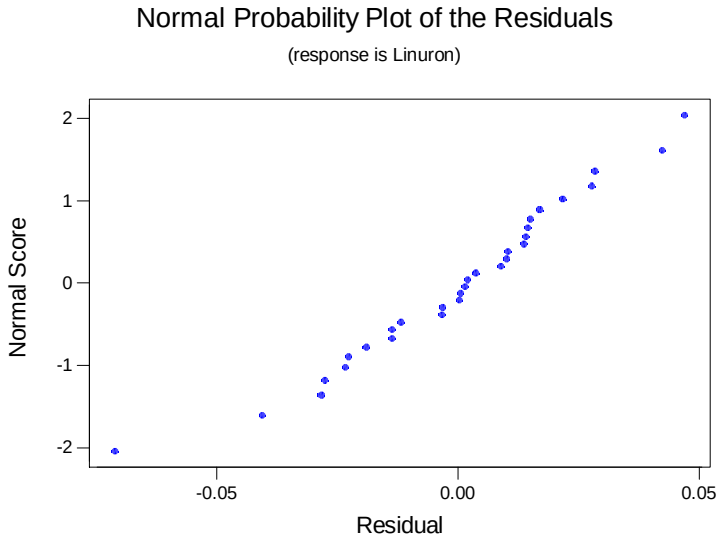
Source	DF	SS	MS	F	P	
Regression	1	0.0032525	0.0032525	5.14	0.031	
Residual Error	28	0.0177292	0.0006332			
Lack of Fit	8	0.0121294	0.0015162	5.42	0.001	**
Pure Error	20	0.0055998	0.0002800			
Total	29	0.0209816				

Unusual Observations

Obs	Week	Linuron	Fit	SE Fit	Residual	St Resid
11	3.0	16.0991	16.1703	0.0054	-0.0712	-2.90R
29	12.0	16.1933	16.1463	0.0090	0.0470	2.00R

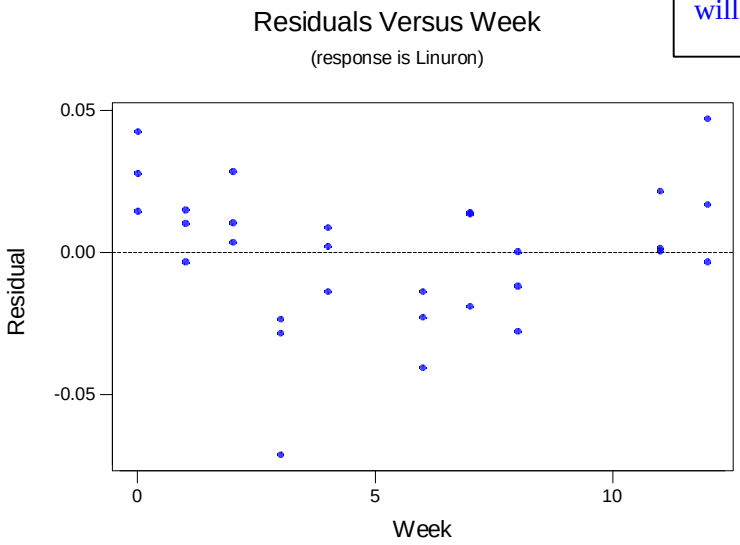
R denotes an observation with a large standardized residual

Normplot of Residuals for Linuron



Residuals from Linuron vs Week

Curvature is apparent, however, a quadratic will not be fit.




```
Do you want to remove any data points? (yes OR no)
n

Should a quadratic be fit? (yes OR no)
n
```

- Power analysis for t-test of slope less than zero

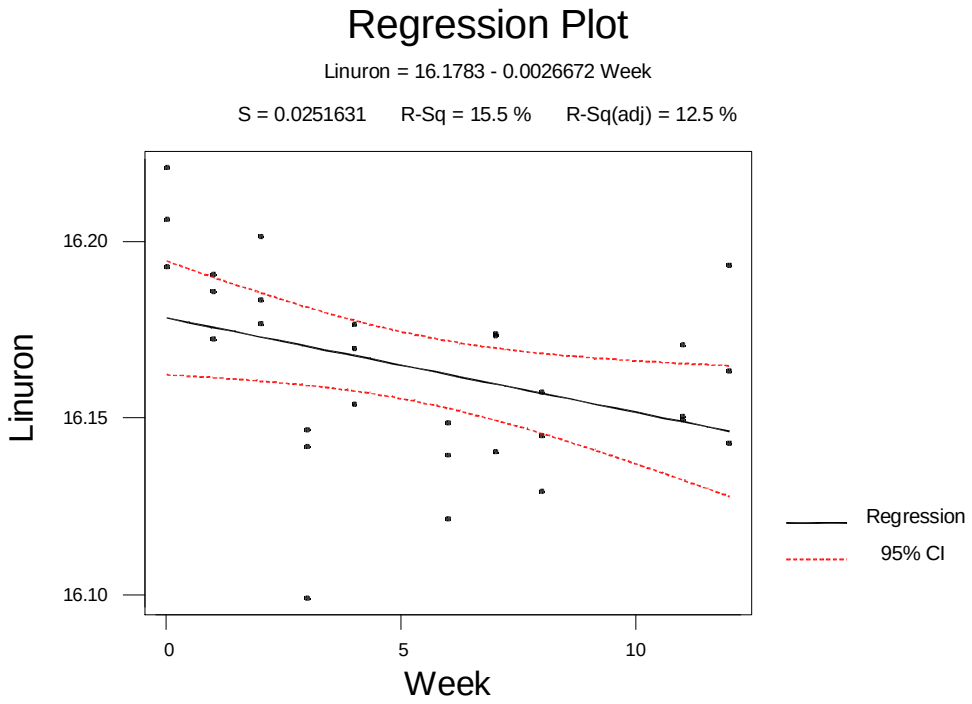
Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0251631

Sample
  Size   Power  Difference
    28  0.9900     -0.0194
```

- That means we would detect a mean of 16.099 as significantly less than ln(10000000) = 16.118 or a change of 9807870 from 10000000 = 1.9% loss.
- Fit 95% confidence bands about the fitted simple linear model



- **Conclusion – stable for 12 weeks.**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Linuron in-life test solution samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Linuron dissolved in corn oil

TEST SOLUTION, SAMPLE CUSTODY. AND PROCESSING:

Test solution samples were prepared by the EDSP Chemical Repository, Sequim, WA, using linuron (CF 1824, Chem Service lot # 273-81B, expiration date 11/05) dissolved in Mazola corn oil (corn oil was from containers with the following expiration dates: 06/12/03, 01/01/04, and 04/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time.

Test solutions of linuron (CAS 330-55-2) supporting EDSP WA 2-14 were made on 1/22/03 at two test concentrations (10 mg/mL and 20 mg/mL) for male-only rat exposures. The 10 mg/mL concentration was prepared by weighing 2.0 g of linuron into a 250 mL, wide-mouth, amber glass bottle and adding 184 g corn oil to obtain the desired concentration. The 20 mg/mL concentration was prepared by weighing 4.0 g of linuron into a 250 mL, wide-mouth, amber glass bottle and adding 182 g corn oil to obtain the desired concentration. The samples were stirred and stored in a refrigerator prior to shipping. Samples were collected on 01/23/03 (Table 1) to verify the test concentrations. Replicate 1 samples were shipped on 01/23/03 and Replicate 2 and 3 samples were shipped on 01/27/03.

The test solution was sampled five times during the male test (01/26/03, 02/02/03, 02/09/03, 02/16/03, 02/23/03). Data are reported in Table 2. Table 3 provides results of analysis of remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test.

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:
Test solution samples analyzed to verify test concentrations were stirred and 1 mL sampled from the middle of the container and transferred to a 60 mL, tared, amber glass bottle. Sample weight was determined gravimetrically. 50 mL acetonitrile (ACN, JT Baker lot # 448346) was added and the container agitated. Then, 0.01 mL (10 mg/mL concentration) or 0.005 mL (20 mg/mL concentration) was transferred to an auto sampler vial with either 0.99 mL or 0.995 mL, respectively of 60% ACN in water. This solution was analyzed on the high-performance liquid chromatograph (HPLC) using an ultraviolet/visible (UV/VIS) detector at the 250 nm wavelength. A 60:40% ACN:water (v:v) buffer was used as an eluent at 1.5 mL/min. Separation was attained using a Supelco petroleum aromatic hydrocarbon (PAH) column (a C-18 column). Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1192, A-E.

In-life and Returned Container Samples:
Samples were returned from RTI on 03/04/03 for male rat assays (received at Battelle, Sequim, WA, on 03/05/03). In-life samples and remaining formulation samples were removed from the refrigerator and allowed to warm to ambient room temperature. On 05/29/03, a 1.0 mL subsample from the containers was collected, placed in a tared, 60 mL, amber glass bottle, and the sample weight determined gravimetrically. 50 mL ACN (JT Baker lot # Y02820) was added, and the container vigorously agitated for two minutes. Then, 0.01 mL was transferred to an auto sampler vial with 0.99 mL 60% ACN in water. This solution was analyzed on the HPLC using a UV/VIS detector at the 250 nm wavelength. A 60:40% ACN:water (v:v) buffer was used as an eluent at 1.5 mL/min. Separation was attained using a Supelco PAH column (a C-18 column). Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1192, A-E. Calibrations from data collected on 04/24/03 were used, although a calibration set was analyzed with the batch of samples analyzed on 05/29/03. Blanks were run with each sample batch and an initial calibration verification (ICV) sample and a continuing calibration verification (CCV) sample were analyzed with each sample set. HPLC-run data are stored on computer WV04738. A corn-oil blank was analyzed with the samples.

SAMPLE ANALYSIS: The samples were analyzed by a modified SW 846 method, 8316, using an HPLC with a UV/VIS detector at the 250 nm wavelength.

Data Quality Objectives	**Control Limits**
Procedural Blank	<5 X MDL
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: Modified SW 846 method, 8316, using an HPLC with a UV/VIS detector at the 250 nm wavelength.

CALIBRATION: Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1192, A-E. Calibrations from data collected on 04/24/03 were used, although a calibration set was analyzed with the batch of samples analyzed on 05/29/03.

CONTINUING STANDARD RECOVERY: Percent recovery results for two initial and three CCV samples analyzed with the in-life sample data set ranged from 96% to 101% with a mean recovery of 98%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK: Linuron was not detected above the detection limit in the two blanks analyzed with the test solution and in-life samples.

DETECTION LIMIT:

The linuron detection limit was 248 µg/mL as determined by an MDL study using the low calibration standard (49.6 µg/mL) reported with the data. No

data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSDs) for the two test solutions ranged from 1.81 to 1.83.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of Linuron Test Solution Concentrations Prepared on 01/22/2003 and Analyzed on 01/23/03

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	% RSD	% of Nominal
	Blank	0.248 U			
10 mg/mL	2-14-D-M R-1	10.3			
10 mg/mL	2-14-D-M R-2	10.7	10.5	1.81	105%
10 mg/mL	2-14-D-M R-3	10.5			
20 mg/mL	2-14-E-M R-1	19.7			
20 mg/mL	2-14-E-M R-2	20.3	20.1	1.83	101%
20 mg/mL	2-14-E-M R-3	20.4			

Table 2. Linuron In-life Sample Concentrations

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
1-26-03	3/5/03	5/29/03	10 mg/mL	1-26-03 D-M	12.3	123%
2-2-03	3/5/03	5/29/03	10 mg/mL	2-2-03 D-M	10.2	102%
2-9-03	3/5/03	5/29/03	10 mg/mL	2-9-03 D-M	10.8	108%
2-16-03	3/5/03	5/29/03	10 mg/mL	2-16-03 D-M	9.90	99%
2-23-03	3/5/03	5/29/03	10 mg/mL	2-23-03 D-M	10.4	104%
1-26-03	3/5/03	5/29/03	20 mg/mL	1-26-03 E-M	19.4	97%
2-2-03	3/5/03	5/29/03	20 mg/mL	2-2-03 E-M	19.0	95%
2-9-03	3/5/03	5/29/03	20 mg/mL	2-9-03 E-M	19.7	99%
2-16-03	3/5/03	5/29/03	20 mg/mL	2-16-03 E-M	19.8	99%
2-23-03	3/5/03	5/29/03	20 mg/mL	2-23-03 E-M	21.2	106%

Table 3. Linuron Post-Test Sample Concentrations for Formulations Returned to Battelle from RTI

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
1/22/03	3/5/03	5/29/03	10 mg/mL	Rec. 2-14-D-M Rep-3	11.9	119%
1/22/03	3/5/03	5/29/03	20 mg/mL	Rec. 2-14-E-M Rep-3	19.4	97%

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Methoxychlor in Mazola Corn Oil

November 10, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory
1529 West Sequim Bay Road
Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology
Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Methoxychlor in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Methoxychlor in Mazola Corn Oil

Parameter	Chemical
Compound Name	Methoxychlor
CAS #	72-43-5
Central File No.	CF-1839
Initial Receipt Date	6/13/02
Expiration Date	4/2006
Manufacturer	Sigma
Lot Number	049H1328
Battelle Study #	WA 2-14-02-01
Method	SW 846, 8015B Modified

Executive Summary

The chemical purity of methoxychlor determined by the manufacturer was 95.2%. The purity result from Battelle-Sequim by GC-FID was determined to be 89.7%. Two concentrations of methoxychlor, 5 and 10 mg/mL, were tested for stability in corn oil. Observed concentrations for both tests dropped below 90% of the target concentration within 0 to 7 days after initiation of the stability trial. Thus, the average day 0 concentration was used as the target concentration for testing stability. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of methoxychlor was expected to stay greater than or equal to 90% of the average day 0 concentration for up to an estimated 35 to 40 days. Thus, stability testing of the methoxychlor stock solution in corn oil was considered stable at the 5 and 10 mg/mL concentrations for the biological test duration of 4.5 weeks.

Mazola corn oil (expiration dates 4-03 and 9-03) was purchased on 9-04-01 and 6-17-02 from local grocery stores, Mark and Pack and Quality Foods Center respectively, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 6-17-02 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn oil with an expiration date of 4-03 was 2.07 meq/kg (RSD = 5.9%). The average peroxide number in the Mazola corn oil with an expiration date of 9-03 was 1.38 meq/kg (RSD = 7.8%). This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on the target concentration ranged from 90% to 109%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA 2-14-02-01, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of methoxychlor (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_Methoxychlor-cornoil.doc, PSTP_ WA-2-14_Methoxychlor-cornoil.doc, DSUM_ WA-2-10_2-14_2-23.xls, and DAF_WA-2-10_2-14_2-23.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, methoxychlor, (CAS No. 72-43-5) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Methoxychlor was purchased from Sigma and lot number 049H1328 was initially received on 6/13/02 with an expiration date of 4/2006 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1839) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Corn oil (expiration dates 4-03 and 9-03) was purchased on 9-04-01 and 6-17-02 from local grocery stores, Mark and Pack and Quality Foods Center respectively, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 6-17-02 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-01

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Methoxychlor (MSL CF 1839)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 5 mg/mL and 10 mg/mL

*Consider if analysis method detection limit which may be determined in Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Planned/proposed test duration: 4.5 weeks

Chemical Information

Chemical Name: Methoxychlor

CAS: 72-43-5

Any known purity information: may refer to attached documentation

Manufacturer's Purity Information: 95.2% pure

Any known stability information: may refer to attached documentation

Manufacturer's Stability Information: stable

Desired purity (%) for test? 95% or greater

Figure 1. EDSP Requisition Form for Methoxychlor

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Methoxychlor
CAS #	72-43-5
Central File No.	CF-1839
Initial Receipt Date	6/13/02
Expiration Date	4/2006
Manufacturer	Sigma
Lot Number	049H1328
Manufacturer's Purity	95.2%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA 2-14-02-01
Method	SW 846, 8015B Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak, and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted by making a solution in hexane of about 100 µg/mL. This matrix was then run on a gas chromatograph with a flame ionization detector (GC-FID). A hexane blank was also run on the GC-FID. The purity was determined by first identifying the peaks in the chromatogram of the methoxychlor that were the same as the peaks in the analysis of the blank hexane sample. The areas associated with these common peaks were then eliminated by inhibiting integration and the remaining peaks were reported as a percentage of the total peak area. The percentage associated with the largest peak represented the purity of methoxychlor. The GC was set up with an auto sampler and a 30 m x 0.25 mm, DB-5 capillary column. The temperature program was set to start at 50 ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and detector at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. Stock solutions were prepared to arrive at the chemical concentrations requested for stability analyses (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

Methoxychlor stock matrices were prepared on 6-18-02 for testing as described in Table 2. Briefly, for the 5 mg/mL methoxychlor, 0.2518 g was weighed into a 50 mL Class A volumetric flask and corn oil was added to the 50 mL mark. The solution was agitated by hand shaking for approximately five minutes until all of the methoxychlor was dissolved. For the

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA 2-14-02-01 12 Weeks	Methoxychlor	5 mg/mL	1839-1a-1	0.2518 g in 50 mL corn oil
		10 mg/mL	1839-1a-2	0.5006 g in 50 mL corn oil

10 mg/mL methoxychlor, 0.5006 g was weighed into a 50 mL Class A volumetric flask and corn oil was added to the mark. The solution was agitated in a similar manner until all of the chemical was dissolved. All solutions were transferred to ashed, amber bottles. Bottles were labeled and stored at 4ºC ± 2ºC for the duration of the test.

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by chromatographic analysis. Triplicate aliquots of each concentration were tested. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

Methoxychlor stock solution was sampled by weighing ~1 g of sample into a 30 mL amber, ashed vial and adding 25 mL of hexane using a volumetric pipette. For samples 1839-1a-1 and 1839-1a-2 analysis was then conducted by adding 0.1 mL of the hexane solution and 0.02 mL of internal standard, 5a androstane, and 0.88 mL of hexane to the GC auto sampler vial. A corn oil blank was prepared the same way. This solution was then run on the GC-FID for quantification. The major peak determined during the purity analysis of methoxychlor was used for this analysis. Continuing calibration verification (CCV) samples were analyzed to demonstrate on-going calibration accuracy.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a GC-FID purity scan on the methoxychlor. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for methoxychlor and several very small peaks. The area of the methoxychlor peak was 89.7% of the total area of all peaks in the chromatogram. Chemical purity of methoxychlor determined by the manufacturer was 95.2% (Appendix A). The observed difference in purity results may be due to the difference in methods.

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 6-18-02. Chemical concentration was determined 11 times over a period of 12 weeks. The analytical and QC results are presented in Appendix C. A single preparation blank was analyzed with every batch for quality control purposes. There were no detectable concentrations of methoxychlor in the blanks. CCV results ranged from 87.4% to 112%. Internal standards were analyzed with each sample and these results ranged from 97.7% to 111%. The MDL was 115 µg/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg as required for biological testing (Appendix C). The average peroxide number in the Mazola corn oil with an expiration date of 4-03 was 2.07 meq/kg (RSD = 5.9%). The average peroxide number in the Mazola corn oil with an expiration date of 9-03 was 1.38 meq/kg (RSD = 7.8%).

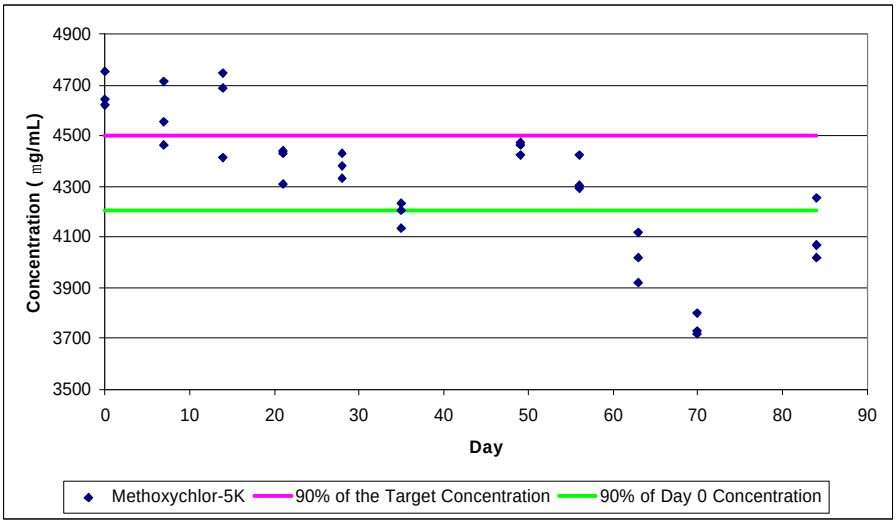
3.3 Statistical Results of Stability Trial

A plot of methoxychlor with a target concentration of 5,000 µg/mL against time shows a significant decline in concentration (Figure 2). All data points were less than 90% of the target concentration after three weeks. Thus, the average day 0 concentration of 4673 µg/mL was tested for stability. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of methoxychlor was expected to stay greater than or equal to 90% of the average day 0 concentration for up to an estimated 40 days (Table 3). Thus, this stock solution was considered stable for the biological test duration of 4.5 weeks. The complete statistical analysis is presented in Appendix D.

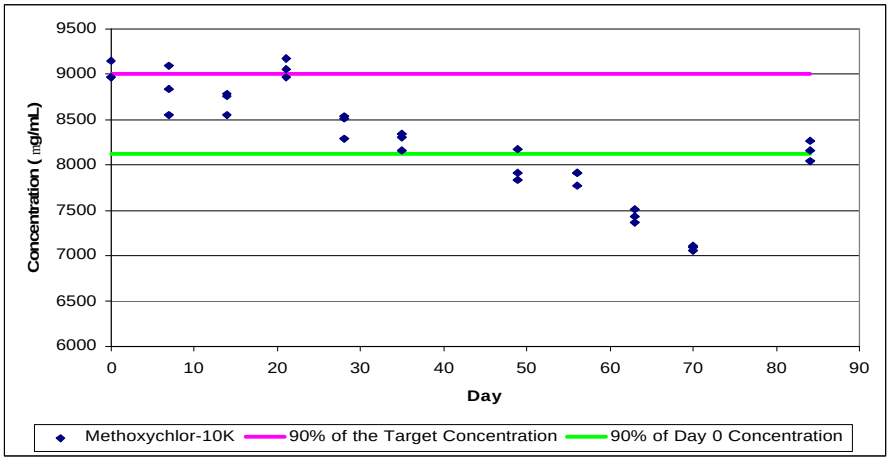
All observations of methoxychlor with a target concentration of 10,000 µg/mL were less than 90% of the target concentration after four weeks. Again, the average day 0 concentration of 9027 µg/mL was tested for stability (Figure 2). Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of methoxychlor was expected to stay greater than or equal to 90% of the average day 0 concentration for an estimated 35 days (Table 3). Thus, this stock solution was considered stable for the biological test duration of 4.5 weeks. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses based on target concentrations ranged from 90% to 109%. The complete analysis is presented in Appendix E.



A



B

Figure 2. Observed Concentration of Methoxychlor with a Target Concentration of 5,000 mg/mL (A) and 10,000 mg/mL (B) Against Time

Table 3. Summary of Statistical Results for Methoxychlor

WA 2-14-02-01 **Statistical Analysis conducted by Valerie Cullinan** **Using Minitab Version 13.32, Minitab Inc., 1999.**	**1839-1a-1** **Methoxychlor-5K**	**1839-1a-2** **Methoxychlor-10K**
Target Concentration (μg/mL)	5000	10000
Number of determinations	1	1
Number of days tested	84	84
Number of replicates per day	3	3
Number of outliers removed	0	0
Number of observations removed	0	0
Overall Mean Concentration	4319	8259
95% Upper CL	4402	8445
error degrees of freedom	32	32
1-sample t-test of Ho: μ >= Target	S[a]	S
estimated intercept of ln(concentration) against time	8.4447	9.1075
estimated slope of ln(concentration) against time	-0.0020	-0.0024
standard error of slope	0.0003	0.0003
error degrees of freedom	31	31
Significance test of lack-of-fit for final model	S	S
Significance test of Ho: β = 0 vs. H1: β = 0	S	S
Lower 95% CL of β	-0.003	-0.003
Upper 95% CL of β	-0.001	-0.002
Maximum Percent Loss (using LCL)	2.0%	2.4%
Mean Percent Loss (using bhat)	1.6%	1.9%
LN(90% of Target)	8.4118	9.1050
Number of days until at 90% of Target (using LCL)	13	1
Conclusion using Target Concentration:	**Stable for 1 wks**	**Stable for 0 wks**
Average Day 0 Concentration	4673	9027
LN(90% of Day 0 Concentration)	8.3441	9.0026
Number of days until at 90% of Day 0 Concentration (using LCL)	40	35
Conclusion using Day 0 Concentration:	**Stable for 4.5 wks**	**Stable for 4.5 wks**

[a] Significant at α = 0.05

4.0 CONCLUSIONS

The stated purity of methoxychlor by the manufacturer was 95.2%; Battelle-Sequim determined the compound to be 89.7% pure. Stability testing of methoxychlor in corn oil concluded that the chemical was stable at the 5 mg/mL and 10 mg/mL concentrations for the required biological testing duration of 4.5 weeks when compared to the average day 0 concentration, but not the nominal concentration.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 90% to 109%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

SIGMA

CF#1839

Certificate of Analysis

TEST	LOT (049H1328) RESULTS
Product Name	Methoxychlor
Product Number	M1501
CAS Number	72435
Formula	$C_{16}H_{15}Cl_3O_2$
Formula Weight	345.7
APPEARANCE	LIGHT ORANGE POWDER WITH A LIGHT TAN CAST
SOLUBILITY	CLEAR FAINT YELLOW SOLUTION AT 200 MG PLUS 4.0 ML OF ETHANOL
IR SPECTRUM	CONSISTENT WITH STRUCTURE
PURITY BY GAS CHROMATOGRAPHY	95.2%
QC ACCEPTANCE DATE	APRIL 1999

David Feldker, Manager
Analytical Services

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Methoxychlor

Chemical Name: Methoxychlor (MSL CF Login 1839)

CAS Number: 72-43-5

Lot Number: 049H1328, 2 100g bottles, stored at RT in Bldg5 Rm 219

Expiration date: 4/06

Manufacturer's Purity Information: 95.2%

Manufacturer's Stability Information: stable

MSL Purity Results:
Purity (%) To be determined at MSL by GC-FID scan

MDL has not been determined.

Bioassay Information: Pesticide LD50 (oral rat) 6000 mg/kg

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Methoxychlor

CAS: 72-43-5

Carrier(s): Mazola corn oil

Concentrations/Dilution Series: 5 and 10 mg/mL

Below MDL determined in Purity Analysis?

In vitro or in *vivo tests*? *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Planned/Proposed test duration: 4.5 weeks

Design of Stability Test: 5 and 10 mg/mL in glass at 4 deg. C in the dark for 12 weeks, analyzed weekly in triplicate by GC detector

Number of replicates: 3

Duration: 12 weeks, sampling each week

Other factors:
Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:
Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
  - Chemical repository confirmatory test results of chemical identity and purity;
  - Chemical repository test results of lot-to-lot variation in chemical purity;
  - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. Methoxychlor concentration in Mazola Corn Oil (µg/mL)

Target Conc.	Sample ID	Date	Methoxychlor	Average	RSD	Recovery[1]
5000 ug/ml	1839-1a-1-1 R-1	6/18/2002	4641			
5000 ug/ml	1839-1a-1-1 R-2	6/18/2002	4754	4673	1.51%	93.5%
5000 ug/ml	1839-1a-1-1 R-3	6/18/2002	4623			
10000 ug/ml	1839-1a-2-1 R-1	6/18/2002	8966			
10000 ug/ml	1839-1a-2-1 R-2	6/18/2002	8967	9027	1.16%	90.3%
10000 ug/ml	1839-1a-2-1 R-3	6/18/2002	9147			
blank	Corn Oil (T=0)	6/19/2002	115 U			
5000 ug/ml	1839-1a-1-2 R-1	6/25/2002	4558			
5000 ug/ml	1839-1a-1-2 R-2	6/25/2002	4716	4579	2.80%	91.6%
5000 ug/ml	1839-1a-1-2 R-3	6/25/2002	4462			
10000 ug/ml	1839-1a-2-2 R-1	6/25/2002	8550			
10000 ug/ml	1839-1a-2-2 R-2	6/25/2002	9101	8830	3.12%	88.3%
10000 ug/ml	1839-1a-2-2 R-3	6/25/2002	8840			
blank	Corn Oil (week 1)	6/25/2002	115 U			
5000 ug/ml	1839-1a-1-3 R-1	7/2/2002	4414			
5000 ug/ml	1839-1a-1-3 R-2	7/2/2002	4688	4617	3.86%	92.3%
5000 ug/ml	1839-1a-1-3 R-3	7/2/2002	4748			
10000 ug/ml	1839-1a-2-3 R-1	7/2/2002	8554			
10000 ug/ml	1839-1a-2-3 R-2	7/2/2002	8788	8701	1.47%	87.0%
10000 ug/ml	1839-1a-2-3 R-3	7/2/2002	8760			
blank	Corn Oil (week 2)	7/2/2002	115 U			
5000 ug/ml	1839-1a-1-4 R-1	7/9/2002	4432			
5000 ug/ml	1839-1a-1-4 R-2	7/9/2002	4310	4394	1.66%	87.9%
5000 ug/ml	1839-1a-1-4 R-3	7/9/2002	4441			
10000 ug/ml	1839-1a-2-4 R-1	7/9/2002	9058			
10000 ug/ml	1839-1a-2-4 R-2	7/9/2002	9171	9063	1.16%	90.6%
10000 ug/ml	1839-1a-2-4 R-3	7/9/2002	8961			
blank	Corn Oil (week 3)	7/9/2002	115 U			
5000 ug/ml	1839-1a-1-5 R-1	7/16/2002	4333			
5000 ug/ml	1839-1a-1-5 R-2	7/16/2002	4428	4381	1.08%	87.6%
5000 ug/ml	1839-1a-1-5 R-3	7/16/2002	4383			
10000 ug/ml	1839-1a-2-5 R-1	7/16/2002	8506			
10000 ug/ml	1839-1a-2-5 R-2	7/16/2002	8284	8444	1.65%	84.4%
10000 ug/ml	1839-1a-2-5 R-3	7/16/2002	8541			
blank	Corn Oil (week 4)	7/16/2002	115 U			
5000 ug/ml	1839-1a-1-6 R-1	7/23/2002	4132			
5000 ug/ml	1839-1a-1-6 R-2	7/23/2002	4205	4190	1.23%	83.8%
5000 ug/ml	1839-1a-1-6 R-3	7/23/2002	4232			
10000 ug/ml	1839-1a-2-6 R-1	7/23/2002	8302			
10000 ug/ml	1839-1a-2-6 R-2	7/23/2002	8156	8267	1.19%	82.7%
10000 ug/ml	1839-1a-2-6 R-3	7/23/2002	8344			
blank	Corn Oil (week 5)	7/23/2002	115 U			
5000 ug/ml	1839-1a-1-7 R-1	8/6/2002	4475			
5000 ug/ml	1839-1a-1-7 R-2	8/6/2002	4461	4453	0.61%	89.1%
5000 ug/ml	1839-1a-1-7 R-3	8/6/2002	4423			
10000 ug/ml	1839-1a-2-7 R-1	8/6/2002	7841			
10000 ug/ml	1839-1a-2-7 R-2	8/6/2002	7913	7975	2.18%	79.8%
10000 ug/ml	1839-1a-2-7 R-3	8/6/2002	8171			

Table C1. continued

Target Conc.	Sample ID	Date	Methoxychlor	Average	RSD	Recovery[1]
blank	Corn Oil (week 7)	8/6/2002	115 U			
5000 ug/ml	1839-1a-1-8 R-1	8/13/2002	4295			
5000 ug/ml	1839-1a-1-8 R-2	8/13/2002	4302	4340	1.65%	86.8%
5000 ug/ml	1839-1a-1-8 R-3	8/13/2002	4423			
10000 ug/ml	1839-1a-2-8 R-1	8/13/2002	7775			
10000 ug/ml	1839-1a-2-8 R-2	8/13/2002	7916	7867	1.02%	78.7%
10000 ug/ml	1839-1a-2-8 R-3	8/13/2002	7910			
blank	Corn Oil (week 8)	8/13/2002	115 U			
5000 ug/ml	1839-1a-1-9 R-1	8/20/2002	4116			
5000 ug/ml	1839-1a-1-9 R-2	8/20/2002	3922	4018	2.41%	80.4%
5000 ug/ml	1839-1a-1-9 R-3	8/20/2002	4017			
10000 ug/ml	1839-1a-2-9 R-1	8/20/2002	7507			
10000 ug/ml	1839-1a-2-9 R-2	8/20/2002	7363	7434	0.97%	74.3%
10000 ug/ml	1839-1a-2-9 R-3	8/20/2002	7430			
blank	Corn Oil (week 9)	8/20/2002	115 U			
5000 ug/ml	1839-1a-1-10 R-1	8/27/2002	3731			
5000 ug/ml	1839-1a-1-10 R-2	8/27/2002	3719	3750	1.18%	75.0%
5000 ug/ml	1839-1a-1-10 R-3	8/27/2002	3801			
10000 ug/ml	1839-1a-2-10 R-1	8/27/2002	7057			
10000 ug/ml	1839-1a-2-10 R-2	8/27/2002	7087	7085	0.39%	70.9%
10000 ug/ml	1839-1a-2-10 R-3	8/27/2002	7111			
blank	Corn Oil (week 10)	8/27/2002	115 U			
5000 ug/ml	1839-1a-1-12 R-1	9/10/2002	4022			
5000 ug/ml	1839-1a-1-12 R-2	9/10/2002	4067	4115	3.01%	82.3%
5000 ug/ml	1839-1a-1-12 R-3	9/10/2002	4255			
10000 ug/ml	1839-1a-2-12 R-1	9/10/2002	8263			
10000 ug/ml	1839-1a-2-12 R-2	9/10/2002	8047	8157	1.33%	81.6%
10000 ug/ml	1839-1a-2-12 R-3	9/10/2002	8160			
blank	Corn Oil (week 12)	9/10/2002	115 U			

[1] Recovery is relative to the target concentration

U = Not detected at a value greater than the MDL

Table C.2. CCV Data for Methoxychlor Concentration in Mazola Corn Oil

Time	Sample Name	Methoxychlor (µg/mL)	Recovery	PD
T=0	EDSP Mix1 5 ug/ml	4.81	96.2%	3.8%
	EDSP Mix1 5 ug/ml	5.16	103%	3.2%
	EDSP Mix1 5 ug/ml	5.12	102%	2.4%
	EDSP Mix1 5 ug/ml	5.10	102%	2.0%
Week 1	EDSP Mix1 5 ug/ml	4.94	98.8%	1.2%
	EDSP Mix1 5 ug/ml	5.06	101%	1.2%
	EDSP Mix1 5 ug/ml	5.08	102%	1.6%
	EDSP Mix1 5 ug/ml	5.07	101%	1.4%
Week 2	EDSP Mix1 5 ug/ml	4.99	100%	0.2%
	EDSP Mix1 5 ug/ml	5.02	100%	0.4%
	EDSP Mix1 5 ug/ml	4.94	98.8%	1.2%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.6%
Week 3	EDSP Mix1 5 ug/ml	5.00	100%	0.0%
	EDSP Mix1 5 ug/ml	5.13	103%	2.6%
	EDSP Mix1 5 ug/ml	5.05	101%	1.0%
	EDSP Mix1 5 ug/ml	5.07	101%	1.4%
	EDSP Mix1 5 ug/ml	4.88	97.6%	2.4%
Week 4	EDSP Mix1 5 ug/ml	4.85	97.0%	3.0%
	EDSP Mix1 5 ug/ml	5.03	101%	0.6%
	EDSP Mix1 5 ug/ml	4.95	99.0%	1.0%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.6%
Week 5	EDSP Mix1 5 ug/ml	5.00	100%	0.0%
	EDSP Mix1 5 ug/ml	4.80	96.0%	4.0%
	EDSP Mix1 5 ug/ml	4.67	93.4%	6.6%
	EDSP Mix1 5 ug/ml	4.48	89.6%	10.4%
Week 7	EDSP Mix1 5 ug/ml	4.93	98.6%	1.4%
	EDSP Mix1 5 ug/ml	5.25	105%	5.0%
	EDSP Mix1 5 ug/ml	5.62	112%	12.4%
	EDSP Mix1 5 ug/ml	5.52	110%	10.4%
Week 8	EDSP Mix1 5 ug/ml	4.86	97.2%	2.8%
	EDSP Mix1 5 ug/ml	5.31	106%	6.2%
	EDSP Mix1 5 ug/ml	5.30	106%	6.0%
	EDSP Mix1 5 ug/ml	5.47	109%	9.4%
Week 9	EDSP Mix1 5 ug/ml	4.61	92.2%	7.8%
	EDSP Mix1 5 ug/ml	4.84	96.8%	3.2%
	EDSP Mix1 5 ug/ml	4.93	98.6%	1.4%
	EDSP Mix1 5 ug/ml	5.01	100%	0.2%
Week 10	EDSP Mix1 5 ug/ml	4.37	87.4%	12.6%
	EDSP Mix1 5 ug/ml	4.50	90.0%	10.0%
	EDSP Mix1 5 ug/ml	4.53	90.6%	9.4%
	EDSP Mix1 5 ug/ml	4.54	90.8%	9.2%
Week 12	EDSP Mix1 5 ug/ml	4.75	95.0%	5.0%
	EDSP Mix1 5 ug/ml	4.95	99.0%	1.0%
	EDSP Mix1 5 ug/ml	4.97	99.4%	0.6%
	EDSP Mix1 5 ug/ml	4.96	99.2%	0.8%

Text Box C1. Calibration Standard Preparation

Calibration Standard EDSP Mix 1
Calibrations were performed using a five-point calibration curve labeled EDSP Mix 1 A thru E. This mix is used for Atrazine, Fenarimol, p,p'-DDE, Methoxychlor and Vinclozolin analyzed by GC-FID. These standards were made by serial dilutions of standards for each compound. • Atrazine standard was made by weighing 0.0499 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with Methylene chloride and labeled 1826-1-1. • Fenarimol standard was made by weighing 0.0506 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1829B-1. • p,p'-DDE standard was made by weighing 0.0501 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1832-1a-1. • Methoxychlor standard was made by weighing 0.0513 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1808-1-3. • Vinclozolin standard was made by weighing 0.0512 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1779-78. This analysis used an internal standard, in this case 5a androstane, which is made by weighing 0.0511 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane, this is then labeled REP7. The EDSP Mix 1 series (A through E) was made as follows. • Solution A, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 0.02 ml REP7 added to a 10 ml volumetric flask and diluted to the mark with hexane. • Solution B, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution C, 0.25 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution D, 0.1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane. • Solution E, 0.05 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane.

Table C.3. Internal Standards Data for Methoxychlor in Mazola Corn Oil

Sample Name	Date	5A Androstane Recovery
1839-1a-1-1 R-1	6/18/2002	105%
1839-1a-1-1 R-2	6/18/2002	103%
1839-1a-1-1 R-3	6/18/2002	105%
1839-1a-2-1 R-1	6/18/2002	105%
1839-1a-2-1 R-2	6/18/2002	107%
1839-1a-2-1 R-3	6/18/2002	108%
1839-1a-1-2 R-1	6/25/2002	101%
1839-1a-1-2 R-2	6/25/2002	105%
1839-1a-1-2 R-3	6/25/2002	104%
1839-1a-2-2 R-1	6/25/2002	104%
1839-1a-2-2 R-2	6/25/2002	102%
1839-1a-2-2 R-3	6/25/2002	103%
1839-1a-1-3 R-1	7/2/2002	104%
1839-1a-1-3 R-2	7/2/2002	97.7%
1839-1a-1-3 R-3	7/2/2002	100%
1839-1a-2-3 R-1	7/2/2002	104%
1839-1a-2-3 R-2	7/2/2002	102%
1839-1a-2-3 R-3	7/2/2002	102%
1839-1a-1-4 R-1	7/9/2002	103%
1839-1a-1-4 R-2	7/9/2002	103%
1839-1a-1-4 R-3	7/9/2002	101%
1839-1a-2-4 R-1	7/9/2002	99.4%
1839-1a-2-4 R-2	7/9/2002	98.5%
1839-1a-2-4 R-3	7/9/2002	98.7%
1839-1a-1-5 R-1	7/16/2002	107%
1839-1a-1-5 R-2	7/16/2002	105%
1839-1a-1-5 R-3	7/16/2002	104%
1839-1a-2-5 R-1	7/16/2002	103%
1839-1a-2-5 R-2	7/16/2002	110%
1839-1a-2-5 R-3	7/16/2002	103%
1839-1a-1-6 R-1	7/23/2002	107%
1839-1a-1-6 R-2	7/23/2002	105%
1839-1a-1-6 R-3	7/23/2002	105%
1839-1a-2-6 R-1	7/23/2002	106%
1839-1a-2-6 R-2	7/23/2002	103%
1839-1a-2-6 R-3	7/23/2002	106%
1839-1a-1-7 R-1	8/6/2002	102%
1839-1a-1-7 R-2	8/6/2002	102%
1839-1a-1-7 R-3	8/6/2002	102%
1839-1a-2-7 R-1	8/6/2002	103%
1839-1a-2-7 R-2	8/6/2002	102%
1839-1a-2-7 R-3	8/6/2002	102%
1839-1a-1-8 R-1	8/13/2002	103%
1839-1a-1-8 R-2	8/13/2002	105%
1839-1a-1-8 R-3	8/13/2002	105%
1839-1a-2-8 R-1	8/13/2002	106%
1839-1a-2-8 R-2	8/13/2002	102%
1839-1a-2-8 R-3	8/13/2002	103%

Table C3. continued

Sample Name	Sample Name	Sample Name
1839-1a-1-9 R-1	8/20/2002	102%
1839-1a-1-9 R-2	8/20/2002	105%
1839-1a-1-9 R-3	8/20/2002	104%
1839-1a-2-9 R-1	8/20/2002	106%
1839-1a-2-9 R-2	8/20/2002	104%
1839-1a-2-9 R-3	8/20/2002	103%
1839-1a-1-10 R-1	8/27/2002	106%
1839-1a-1-10 R-2	8/27/2002	110%
1839-1a-1-10 R-3	8/27/2002	111%
1839-1a-2-10 R-1	8/27/2002	108%
1839-1a-2-10 R-2	8/27/2002	108%
1839-1a-2-10 R-3	8/27/2002	108%
1839-1a-1-12 R-1	9/10/2002	105%
1839-1a-1-12 R-2	9/10/2002	105%
1839-1a-1-12 R-3	9/10/2002	105%
1839-1a-2-12 R-1	9/10/2002	102%
1839-1a-2-12 R-2	9/10/2002	105%
1839-1a-2-12 R-3	9/10/2002	107%

Table C.4. Peroxide Concentration in Mazola Corn Oil (meq/kg) measured on 6/17/02

Sample	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	0.75	0.005	5.00	0.75		
Mazola Corn Oil Expiration 9-03 R-1	1.6	0.005	5.43	1.47		
Mazola Corn Oil Expiration 9-03 R-2	1.5	0.005	5.32	1.41	1.38	7.8%
Mazola Corn Oil Expiration 9-03 R-3	1.2	0.005	4.75	1.26		
Mazola Corn Oil Expiration 4-03 R-1	2.0	0.005	5.18	1.93		
Mazola Corn Oil Expiration 4-03 R-2	2.2	0.005	5.09	2.16	2.07	5.9%
Mazola Corn Oil Expiration 4-03 R-3	2.5	0.005	5.21	2.11		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-01
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

11/25/2002 11:22:30 AM

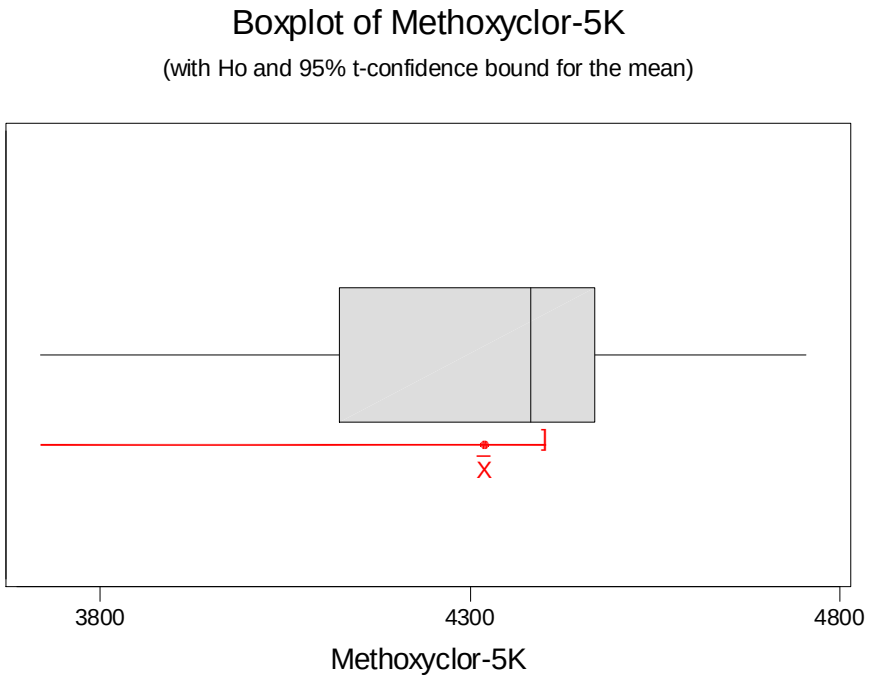
Analysis of Methoxychlor-5k in corn oil

- Test to determine if the data are from a population with mean of 5000.

One-Sample T: Methoxychlor-5K

```
Test of mu = 5000 vs mu < 5000

Variable           N      Mean     StDev   SE Mean
Methoxychlor-     33    4319.0     281.5      49.0

Variable       95.0% Upper Bound        T      P
Methoxychlor-             4402.0   -13.90  0.000
```

t Boxplot of Methoxychlor-5K



- Nonparametric Test for outlier.

```
Outliers are < Median-3*IQD OR > Median+3*IQD
Boundary for outliers are values <    3348.62  and >    5416.88
No outliers
```

- Transform data to natural logarithm and conduct regression analysis.

Week	Rep	Ln(Concentration)
0	1	8.4428
0	2	8.4667
0	3	8.4388
7	1	8.4246
7	2	8.4587
7	3	8.4034
14	1	8.3925
14	2	8.4529
14	3	8.4654
21	1	8.3965
21	2	8.3687
21	3	8.3985
28	1	8.3740
28	2	8.3957
28	3	8.3854
35	1	8.3266
35	2	8.3441
35	3	8.3504
49	1	8.4063
49	2	8.4030
49	3	8.3945
56	1	8.3651
56	2	8.3669
56	3	8.3945
63	1	8.3225
63	2	8.2743
63	3	8.2983
70	1	8.2245
70	2	8.2212
70	3	8.2430
84	1	8.2996
84	2	8.3106
84	3	8.3559

  - Conducts Simple Linear Regression

Regression Analysis: Methoxychlor-5K versus Day

The regression equation is
Methoxychlor-5K = 8.44 - 0.00196 Day

Predictor	Coef	SE Coef	T	P
Constant	8.44471	0.01299	650.13	0.000
Day	-0.0019588	0.0002772	-7.07	0.000

S = 0.04180 R-Sq = 61.7% R-Sq(adj) = 60.5%

Analysis of Variance

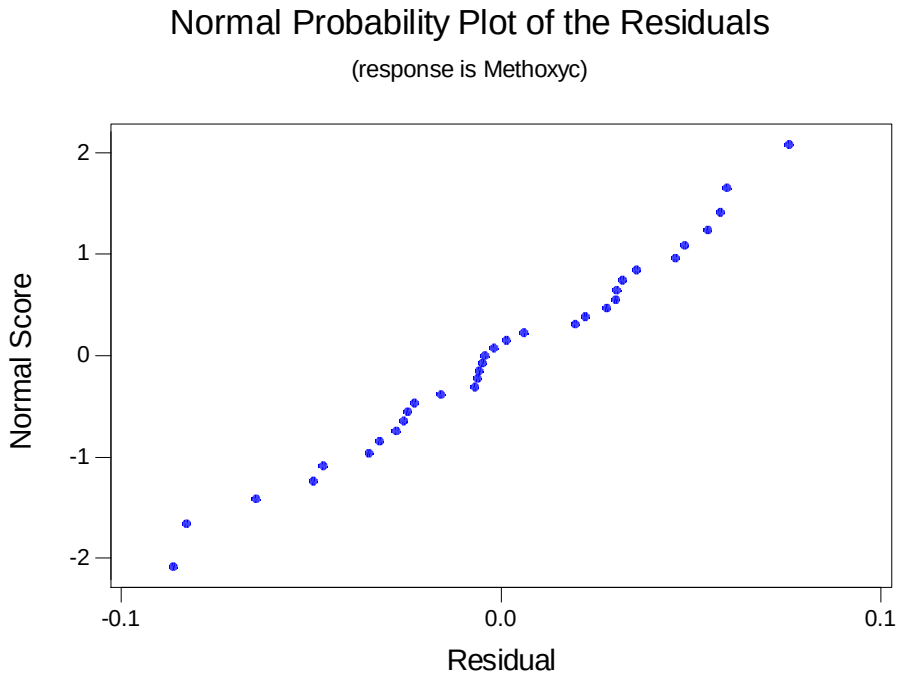
Source	DF	SS	MS	F	P
Regression	1	0.087268	0.087268	49.94	0.000
Residual Error	31	0.054171	0.001747		
Lack of Fit	9	0.044193	0.004910	10.83	0.000
Pure Error	22	0.009978	0.000454		
Total	32	0.141440			

Unusual Observations

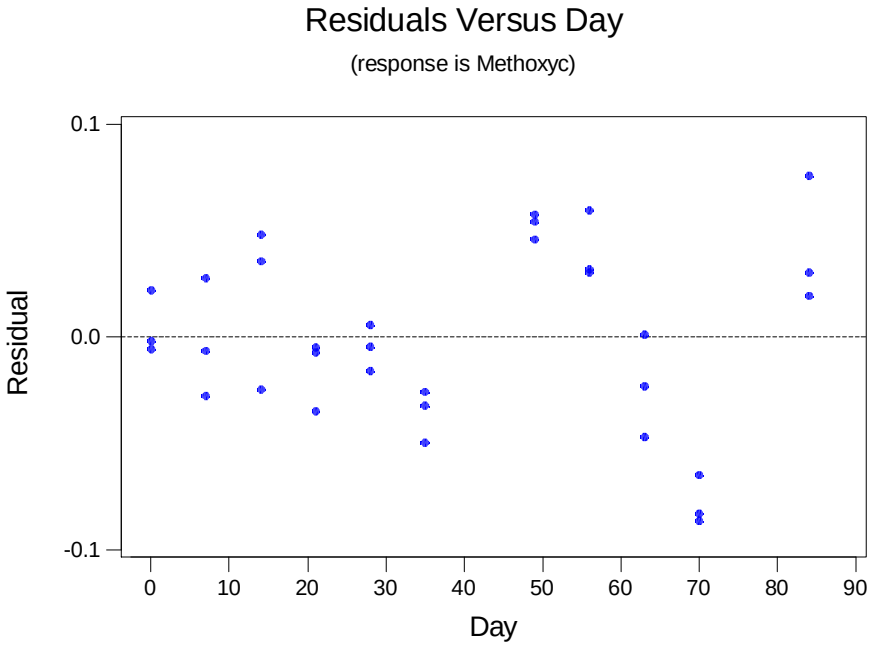
Obs	Day	Methoxychlor	Fit	SE Fit	Residual	St Resid
28	70.0	8.22455	8.30760	0.01130	-0.08305	-2.06R
29	70.0	8.22122	8.30760	0.01130	-0.08638	-2.15R

R denotes an observation with a large standardized residual

Normplot of Residuals for Methoxychlor



Residuals from Methoxychlor vs Day



- Power analysis for t-test of slope less than zero

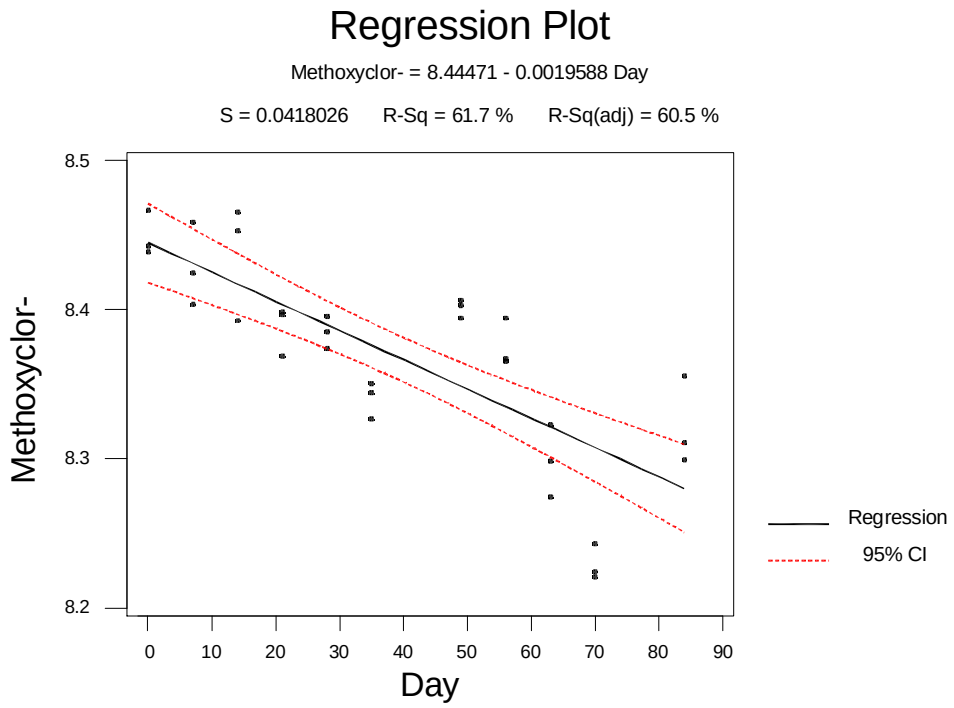
Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0418026

Sample
  Size   Power  Difference
    31  0.9900     -0.0305
```

- That means we would detect a mean of 8.4867 as significantly less than ln(5000) = 8.5172 or a change of 4850 from 5000 = 3.0% loss.

- Fit 95% confidence bands about the fitted simple linear model

Fitted Line Plot: Methoxychlor- versus Day



- **Conclusion – stable for 1 weeks from target concentration.**
- **Conclusion – stable for 4.5 weeks if from average of day 0 concentration (see Excel spreadsheet WA 2-10_WA2-14stability rev 1.xls).**

WA-2-14-02-01
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

11/25/2002 11:22:30 AM

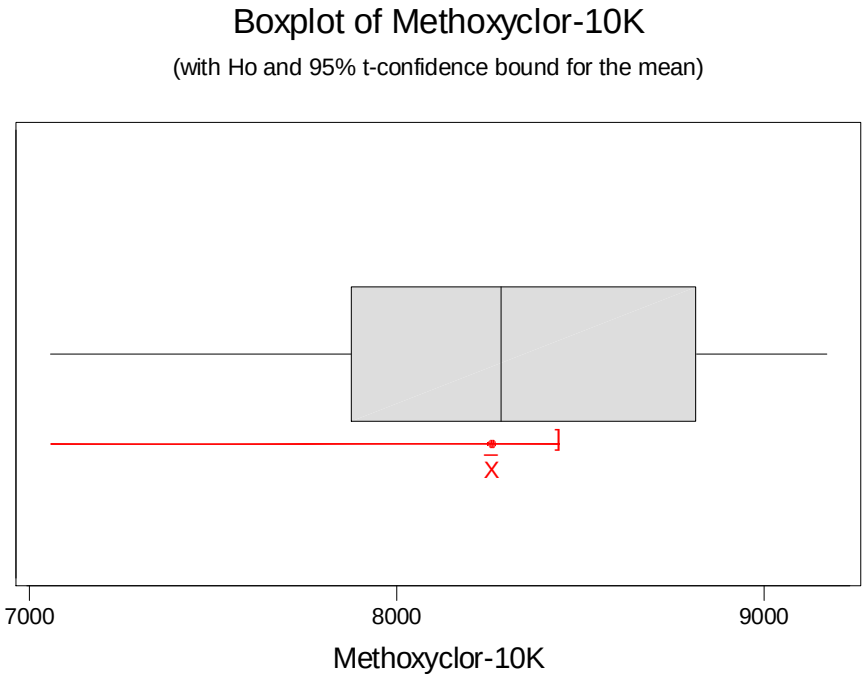
Analysis of Methoxychlor-10k in corn oil

- Test to determine if the data are from a population with mean of 10000.

One-Sample T: Methoxychlor-10K

```
Test of mu = 10000 vs mu < 10000

Variable           N      Mean     StDev   SE Mean
Methoxychlor-     33      8259       630       110

Variable       95.0% Upper Bound        T      P
Methoxychlor-               8445   -15.89  0.000
```

t Boxplot of Methoxychlor-10K



- Nonparametric Test for outlier.

```
Outliers are < Median-3*IQD OR > Median+3*IQD
Boundary for outliers are values <    5469.47  and >    11098.7
No outliers
```

- Transform data to natural logarithm and conduct regression analysis.

Week	Rep	Ln(Concentration)
0	1	9.1012
0	2	9.1013
0	3	9.1212
7	1	9.0537
7	2	9.1162
7	3	9.0870
14	1	9.0541
14	2	9.0812
14	3	9.0779
21	1	9.1114
21	2	9.1238
21	3	9.1006
28	1	9.0486
28	2	9.0221
28	3	9.0527
35	1	9.0242
35	2	9.0065
35	3	9.0293
49	1	8.9671
49	2	8.9762
49	3	9.0084
56	1	8.9586
56	2	8.9766
56	3	8.9759
63	1	8.9237
63	2	8.9043
63	3	8.9133
70	1	8.8617
70	2	8.8660
70	3	8.8694
84	1	9.0195
84	2	8.9930
84	3	9.0070

  - Conducts Simple Linear Regression

Regression Analysis: Methoxychlor-10K versus Day

The regression equation is
Methoxychlor-10K = 9.11 - 0.00235 Day

Predictor	Coef	SE Coef	T	P
Constant	9.10753	0.01442	631.66	0.000
Day	-0.0023535	0.0003077	-7.65	0.000

S = 0.04640 R-Sq = 65.4% R-Sq(adj) = 64.2%

Analysis of Variance

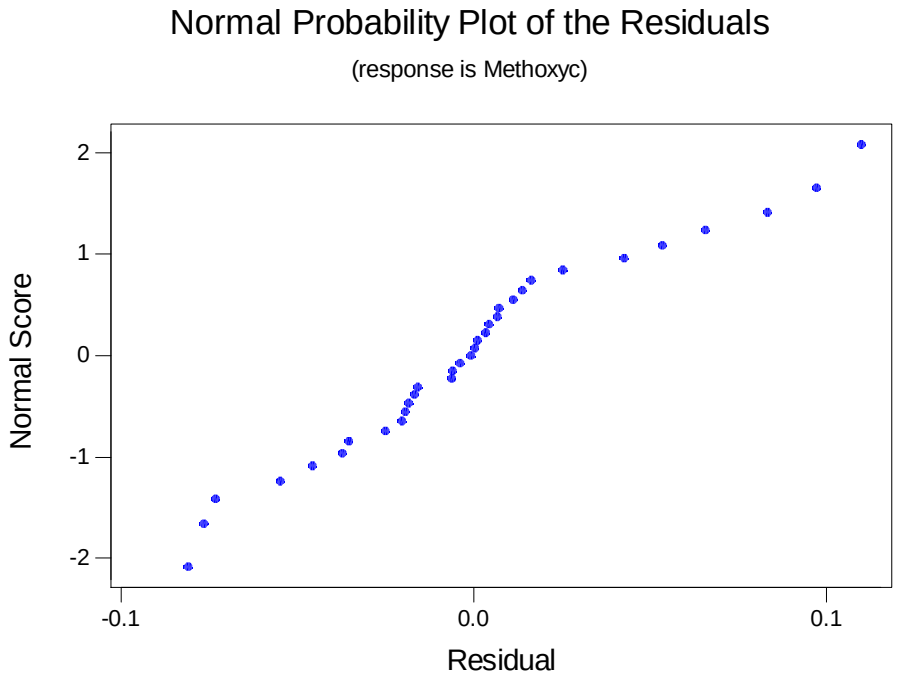
Source	DF	SS	MS	F	P
Regression	1	0.12598	0.12598	58.51	0.000
Residual Error	31	0.06675	0.00215		
Lack of Fit	9	0.06127	0.00681	27.33	0.000
Pure Error	22	0.00548	0.00025		
Total	32	0.19273			

Unusual Observations

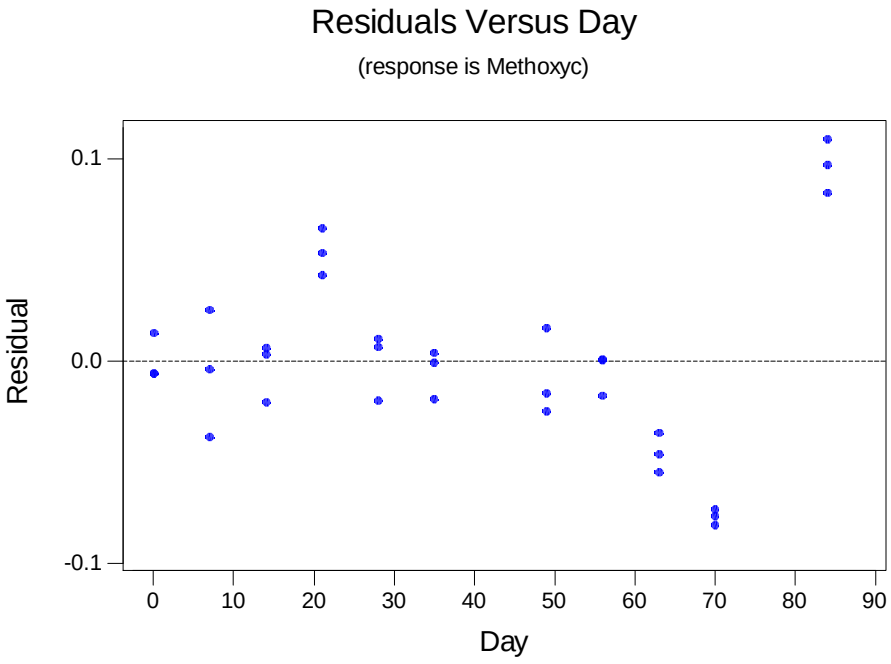
Obs	Day	Methoxychlor	Fit	SE Fit	Residual	St Resid
31	84.0	9.01955	8.90984	0.01608	0.10971	2.52R
33	84.0	9.00696	8.90984	0.01608	0.09712	2.23R

R denotes an observation with a large standardized residual

Normplot of Residuals for Methoxychlor



Residuals from Methoxychlor vs Day



- Power analysis for t-test of slope less than zero

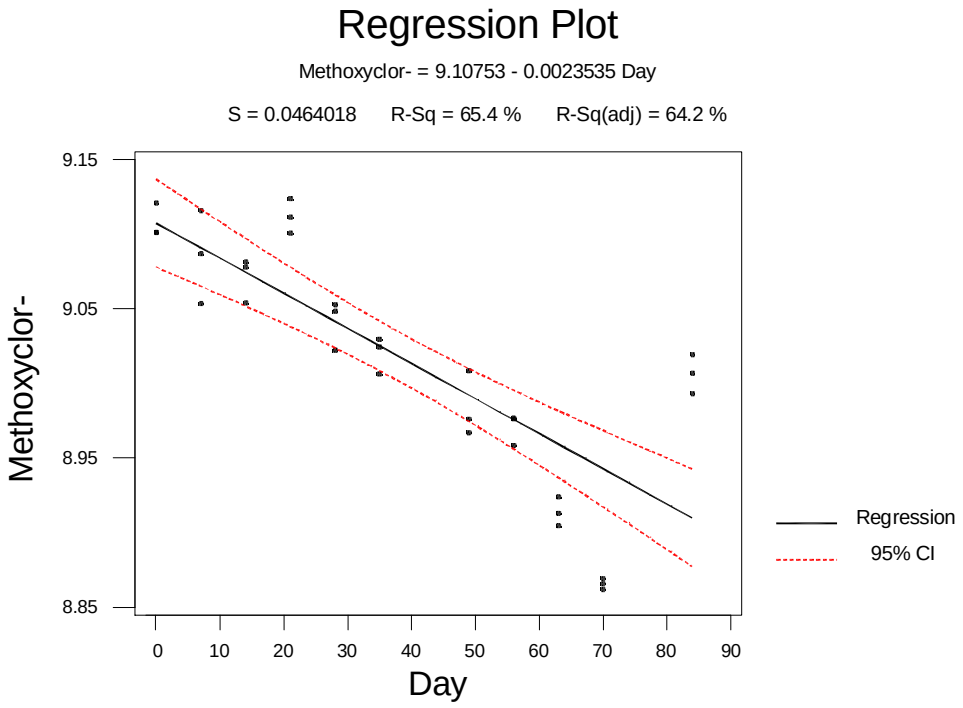
Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0464018

Sample
  Size   Power  Difference
    31  0.9900     -0.0339
```

- That means we would detect a mean of 9.1764 as significantly less than ln(10000) = 9.2103 or a change of 9667 from 10000 = 3.3% loss.

- Fit 95% confidence bands about the fitted simple linear model

Fitted Line Plot: Methoxychlor- versus Day



- **Conclusion – stable for 0 weeks from target concentration.**
- **Conclusion – stable for 4.5 weeks if from average of day 0 concentration (see Excel spreadsheet WA 2-10_WA2-14stability rev 1.xls).**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Methoxychlor in-life test solution samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Methoxychlor in corn oil

TEST SOLUTION SAMPLE CUSTODY AND PROCESSING:

Test solution samples were prepared by the EDSP Chemical Repository, Sequim, WA, using methoxychlor (CF 1839, Sigma lot #49H1328, expiration date 4/06) dissolved in Mazola corn oil (corn oil was from containers with the following expiration dates: 06/12/03, 01/01/04, and 04/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time. Samples were prepared at two test concentrations, 5 mg/mL and 10 mg/mL, for all replicates and exposures unless noted below. The 5 mg/mL concentration was prepared by dissolving 1.05 g of methoxychlor in 185 g of corn oil in a pre-cleaned, amber glass container. The 10 mg/mL concentration was prepared by dissolving 2.10 g of methoxychlor in 184 g of corn oil. Note: the weights used reflect adjustments made for the 95% purity of the methoxychlor.

Samples for female rat exposures were prepared at three different times (Table 1):
Replicate 1 – prepared on 09/09/02 and shipped on 09/10/02
Replicate 2 – prepared on 09/15/02 and shipped on 09/16/02
Replicate 3 – 5 mg/mL concentration only, prepared on 09/15/02 and shipped on 9/16/02 to replace Replicate 1 at the 5 mg/mL concentration, which was not verified upon analysis.

Samples for male rat exposures were prepared at four different times:
Replicate 1 – prepared on 09/09/02 and shipped on 09/26/02
Replicate 2 – prepared on 10/02/02 and shipped on 10/03/02
Replicate 3 – prepared on 10/16/02 and shipped on 10/17/02
Replicate 4 – prepared on 11/03/02 and shipped on 11/04/02.
Results of verification of concentrations for Replicates 1, 2, and 3 are reported in Table 2.

The test solution was sampled four times during the female test (9/18/02, 9/24/02, 10/01/02, and 10/08/02) and four times during the male test (10/07/02, 10/14/02, 10/21/02, and 10/28/02). Data are reported in Table 3 for females and Table 4 for males. Table 5 provides results of analysis of remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test.

Processing
Test Solution Samples for Concentration Verification Prior to Shipping:

The container was sampled prior to shipment. 1 mL triplicate samples were removed and each placed in a tared, 60 mL, amber glass bottle. The weight of

the sample was determined gravimetrically. A 1 g subsample was removed, placed in a 30 mL amber ashed vial, and 25 mL of hexane (JT Baker lot number X40E12) was added and the bottle agitated to mix. Then, 0.1 mL sample and 0.02 mL internal standard, 5a androstane, and 0.88 mL hexane were transferred to an auto sampler vial.

In-life and Returned Container Samples:

In-life and returned containers were analyzed the same way. Some of the returned containers were returned empty, so only containers with sufficient material were analyzed.

The samples were removed from the refrigerator, allowed to warm to room temperature, and then stirred using a magnetic stir bar and stir plate. About 1 mL was sampled and placed in a tared, 30 mL, amber-glass bottle. The weight of the sample was determined gravimetrically. 25 mL of hexane was added and the bottle agitated to mix. Then 0.1 mL was transferred to a 1.8 mL vial with 0.02 mL of internal standard solution containing 5a androstane and 0.88 mL hexane.

SAMPLE ANALYSIS: The samples were analyzed by gas chromatograph (GC) with a flame ionization detector (FID). The GC was set up with an auto sampler and a 30-m x 0.25-mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and the detector temperature at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution.

Data Quality Objectives	Control Limits
Procedural Blank	<5 * MDL
Blank Spike Recovery	40% - 120%
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: GC-FID

CALIBRATION: Calibration with a five-point curve was done using dilutions prepared from standard EDSP Mix 1 (see Appendix C) with a continuing calibration verification (CCV) sample analyzed every 10 samples.

CONTINUING STANDARD RECOVERY: Percent recovery results for initial and CCV samples analyzed with the in-life sample data set ranged from 91% to 117% with a mean recovery of 100%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK: Methoxychlor was not detected above the detection limit in the corn oil blank analyzed with the test solution and in-life samples.

DETECTION LIMIT: The methoxychlor method detection limit (MDL) in corn oil was 115 µg/mL as determined by an MDL study. No data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed. In this analysis, sampling was performed by taking the sample material from flask through to analysis. Analyzing a spiked sample would be no different from analyzing a CCV.

INTERNAL STANDARD: 5a androstane was spiked into each sample and analyzed as the internal standard. Average percent recovery results ranged from 99% to 103%. There were no cases in which the percent recovery of the internal standard exceeded the acceptance range of 40% to 120%.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSD) for the two test solution concentrations for female exposures ranged from 2.06 to 5.65.

The % RSD for the two methoxychlor concentrations for male exposures ranged from 0.600 to 2.46.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of Methoxychlor Test Solution Concentrations for Female Exposures

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	% RSD
R-1; 09/09/02				
5 mg/mL	2-14 –B-F R-1, R-1	N/A		
5 mg/mL	2-14 –B-F R-1, R-2	4.31[(a)]	N/A	N/A
5 mg/mL	2-14 –B-F R-1, R-3	8.59[(a)]	N/A	
10 mg/mL	2-14 –C-F R-1, R-1	9.57		
10 mg/mL	2-14 –C-F R-1, R-2	9.19	9.36	2.06
10 mg/mL	2-14 –C-F R-1, R-3	9.31		
R-2; 09/15/02				
5 mg/mL	2-14 –B-F R-2, R-1	5.12		
5 mg/mL	2-14 –B-F R-2, R-2	4.63	4.94	5.65
5 mg/mL	2-14 –B-F R-2, R-3	5.01		
R-3 09/15/02				
5 mg/mL	2-14 –B-F R-3, R-1	4.66		
5 mg/mL	2-14 –B-F R-3, R-2	4.94	4.87	3.98
5 mg/mL	2-14 –B-F R-3, R-3	5.03		

(a) Concentrations were not as expected, and replacement test solutions (R-3, 9/15/02) were provided.

Table 2. Verification of Methoxychlor Test Solution Concentrations for Male Exposures

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	% RSD
R-1; 09/09/02				
5 mg/mL	2-14 –L-M R-1, R-1	4.76		
5 mg/mL	2-14 –L-M R-1, R-2	4.61	4.69	1.54
5 mg/mL	2-14 –L-M R-1, R-3	4.69		
10 mg/mL	2-14 –M-M R-1, R-1	9.79		
10 mg/mL	2-14 –M-M R-1, R-2	9.58	9.62	1.59
10 mg/mL	2-14 –M-M R-1, R-3	9.50		
R-2; 10/02/02				
5 mg/mL	2-14 –L-M R-2, R-1	4.89		
5 mg/mL	2-14 –L-M R-2, R-2	4.87	4.90	0.600
5 mg/mL	2-14 –L-M R-2, R-3	4.93		
10 mg/mL	2-14 –M-M R-2, R-1	9.71		
10 mg/mL	2-14 –M-M R-2, R-2	9.71	9.85	2.46
10 mg/mL	2-14 –M-M R-2, R-3	10.13		
R-3 10/16/02				
5 mg/mL	2-14 –L-M R-3, R-1	5.38		
5 mg/mL	2-14 –L-M R-3, R-2	5.44	5.48	2.21
5 mg/mL	2-14 –L-M R-3, R-3	5.62		
10 mg/mL	2-14 –M-M R-3, R-1	10.93		
10 mg/mL	2-14 –M-M R-3, R-2	10.86	10.8	0.797
10 mg/mL	2-14 –M-M R-3, R-3	10.75		

Table 3. Methoxychlor In-life Sample – Females

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
09/18/02	10/16/02	11/23/02	5 mg/mL	WA2-14B-F 9-18 Vial	4.61	92%
09/24/02	10/16/02	11/23/02	5 mg/mL	WA2-14B-F 9-24 Vial	4.63	93%
10/01/02	10/16/02	11/23/02	5 mg/mL	WA2-14B-F 10-1 Vial	4.79	96%
10/08/02	10/16/02	11/23/02	5 mg/mL	WA2-14B-F 10-8 Vial	4.93	99%
09/18/02	10/16/02	11/23/02	10 mg/mL	WA2-14C-F 9-18 Vial	9.01	90%
09/24/02	10/16/02	11/23/02	10 mg/mL	WA2-14C-F 9-24 Vial	9.21	92%
10/01/02	10/16/02	11/23/02	10 mg/mL	WA2-14C-F 10-1 Vial	9.26	93%
10/08/02	10/16/02	11/23/02	10 mg/mL	WA2-14C-F 10-8 Vial	9.43	94%

Table 4. Methoxychlor In-life Sample– Males

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. mg/mL)	% of Nominal
10/07/02	11/13/02	11/23/02	5 mg/mL	WA2-14L-M 10-7 Vial	4.72	94%
10/14/02	11/13/02	11/23/02	5 mg/mL	WA2-14L-M 10-14Vial	4.63	93%
10/21/02	11/13/02	12/05/02[(a)]	5 mg/mL	WA2-14L-M 10-21Vial	5.43[(a)]	109%
10/28/02	11/13/02	11/23/02	5 mg/mL	WA2-14L-M 10-28Vial	4.52	90%
10/07/02	11/13/02	11/23/02	10 mg/mL	WA2-14M-M 10-7 Vial	9.23	92%
10/14/02	11/13/02	12/05/02[(a)]	10 mg/mL	WA2-14M-M 10-14Vial	9.85[(a)]	99%
10/21/02	11/13/02	12/05/02[(a)]	10 mg/mL	WA2-14M-M 10-21Vial	9.26[(a)]	93%
10/28/02	11/13/02	11/23/02	10 mg/mL	WA2-14M-M 10-28Vial	9.12	91%

(a) Re-analyzed on 12/05/02

Table 5. Methoxychlor Post-Test Sample Concentrations for Formulations Returned to Battelle from RTI

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
Female Exposures						
09/09/02	10/16/02	11/22/02	5 mg/mL	WA 2-14-B-F Rep1Jar	4.62	92%
09/15/02	10/16/02	11/22/02	5 mg/mL	WA 2-14-B-F Rep2Jar	4.93	99%
09/15/02	10/16/02	11/22/02	10 mg/mL	WA 2-14-C-F Rep2Jar	9.34	93%
Male Exposures						
09/09/02	11/13/02	11/22/02	5 mg/mL	WA 2-14-L-M Rep1Jar	4.57	91%
10/02/02	11/13/02	11/22/02	5 mg/mL	WA 2-14-L-M Rep2Jar	4.70	94%
11/03/02	11/13/02	11/22/02	5 mg/mL	WA 2-14-L-M Rep4Jar	4.62	92%
09/09/02	11/13/02	11/22/02	10 mg/mL	WA 2-14-M-M Rep1Jar	9.12	91%
10/02/02	11/13/02	11/22/02	10 mg/mL	WA 2-14-M-M Rep2Jar	9.42	94%
11/03/02	11/13/02	11/22/02	10 mg/mL	WA 2-14-M-M Rep4Jar	9.28	93%

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-004: Atrazine, DDE, vinclozolin, Methoxychlor, Fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[X]	Protocol
[ ]	SOP	[ ]	Method	[ ]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: 2.3 of protocol WA 2-14 states "an aliquot of each level per formulation will be analyzed"

DEVIATION: Each dose level was tested in the first preparation for each chemical. However, subsequent batches were not always analyzed.

REASON/IMPACT: No impact. Subsequent batches were prepared using the same methods and procedures as the first batches.
PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action required.

ACTIONS TO PREVENT RECURRENCE: Upper management will review the analyses schedule prior to the start of the studies.

Approval:

Michael Blanton,
WAL — Date 11-3-03

Eric Crecelius,
Study Director
Chemical Repository — Date 11-3-03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Phenobarbital in Mazola Corn Oil

November 10, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory
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Submitted to:

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Chemistry Report for WA 2-14
Phenobarbital in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Phenobarbital in Mazola Corn Oil

Parameter	Chemical
Compound Name	Phenobarbital
CAS #	50-06-6
Central File No.	CF-1837
Initial Receipt Date	6/6/2002
Expiration Date	06/06
Manufacturer	Sigma, Inc.
Lot Number	81K2620
Battelle Study #	WA2-14-02-02
Method	SW 846, 8316 Modified

Executive Summary

The chemical purity of phenobarbital was not specified by the manufacturer. The purity result from Battelle-Sequim by HPLC was determined to be 99.1%. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of phenobarbital was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 13 weeks. Thus, stability testing of the phenobarbital stock solution in Mazola corn oil was considered stable at 10 mg/mL for the required testing and holding period of 12 weeks.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 09/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn oil was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on the target concentration ranged from 94% to 103%.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA2-14-02-02, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of phenobarbital (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_phenobarbital-cornoil.doc, PSTP_WA-2-14_phenobarbital-cornoil.doc, DSUM_WA2-14_Phenobarbital-crnoil.xls, and DAF_WA-2-14_Phenobarbital-cornoil.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, phenobarbital, (CAS No. 50-06-6) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Phenobarbital was purchased from Sigma, Inc., and lot number 81K2620 was initially received on 6/6/2002 with an expiration date of 06/06 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1837) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored as a controlled substance in a lockbox at 4°C.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-02

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Phenobarbital (MSL CF 1837)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 10 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Testing/holding duration: 12 weeks

Chemical Information

Chemical Name: Phenobarbital

CAS: 50-06-6

Any known purity information: may refer to attached documentation	None available
Any known stability information: may refer to attached documentation	Manufacturer's Stability Information: stable
Desired purity (%) for test? 95% or greater	

Figure 1. EDSP Requisition Form for Phenobarbital

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Phenobarbital
CAS #	50-06-6
Central File No.	CF-1837
Receipt Date	6/6/2002
Expiration Date	06/06
Manufacturer	Sigma, Inc.
Lot Number	81K2620
Manufacturer's Purity	Purity not specified
Storage Conditions	Cool, dry place at 4 °C
Battelle Study #	WA2-14-02-02
Method	SW 846, 8316 Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak. A manufacturer's certificate of analysis/purity was not available (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted using an high performance liquid chromatography (HPLC) with ultraviolet (UV) absorbance at 225 nm by running standard PP-1189E (5000 ng/ml) in 60% acetonitrile (ACN): 40% de-ionized water solution (v:v). This matrix was run on the HPLC and the purity determined by comparing the peak heights of the peaks in the chromatogram. The HPLC was set up with an auto sampler and a column oven. The column oven temperature was set at 30ºC, and the auto sampler was set to inject 250 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. A stock solution was prepared to arrive at the chemical concentrations requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

A phenobarbital stock matrix was prepared on 10/15/02 for testing as described in Table 2. The first analysis was done 10/16/02; this was considered the start of the test. Briefly, for the 10 mg/mL phenobarbital, 2 g was weighed into 250 mL wide-mouth amber glass bottle, 184 g of Mazola corn oil was added, the sample was stirred over night, and stored in a refrigerator at 4°C ± 2°C.

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA2-14-02-02 12 Weeks	Phenobarbital	10 mg/mL	1837-1-2	2 g in 184 g Mazola corn oil

The density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL, respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by chromatographic analysis. Triplicate aliquots were tested for the 10 mg/mL concentration. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

Sample analyses were conducted by first placing the container on a magnetic stir plate, adding a stir bar and stirring overnight. After stirring, 1 mL triplicate samples were removed and each was placed in a tared 60 mL amber glass bottle. The weight of the sample was determined gravimetrically. Then, 50 mL of ACN was added and the bottle agitated to mix. After mixing, 0.01 mL was transferred to an auto sampler vial with 0.99 mL of 60% ACN in water. The samples were analyzed using an HPLC with a UV/VIS detector at the 225 nm wavelength. A 60:40% ACN:water mix (v:v) was used as the eluent at 1.5 mL/minute. Separation was attained using a Supelco (25 cm x 4.8 mm) C-18 column. For samples analyzed using the HPLC system, data were stored in MSL5, room 219 on the computer with a property number of WV04738.

Calibrations using a five-point calibration curve were performed using dilutions prepared from standard PP-1189, which is itself a serial dilution of PP-1183 which was made by weighing 0.1000 g of phenobarbital into a 100 mL volumetric flask. This was then diluted to the 100 mL mark with ACN. The PP-1189 series (A through E) was made using the following amounts of PP-1183 which was then diluted to the 100 mL mark with a 60:40% ACN:water mix (v:v): PP-1189A was 0.2 mL of PP-1183, PP-1189B was 0.05 mL of PP-1183; PP-1189C was 0.02 mL of PP-1183; PP-1189D was 0.005 mL of PP-1183; and PP-1189E was 0.5 mL of PP-1183.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a HPLC purity scan on the phenobarbital. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for phenobarbital and several very small peaks. The area of the phenobarbital peak indicated the material was 99.1% pure. Chemical purity of phenobarbital was not documented by the manufacturer (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 10/16/02. Chemical concentrations were determined 10 times from 10/16/02 to 01/07/03. The analytical and quality control (QC) results are presented in Appendix C. A single preparation blank was analyzed with every batch for QC purposes. There were no concentrations of phenobarbital in the blanks above the detection limit. Continuing calibration verification (CCV) results ranged from 87.4% to 110%. Internal standards were not analyzed. The MDL was 250,000 ng/mL. The dilution factor of the formulation can be taken into account, and thus, the MDL of the diluted sample was 50 ng/mL.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

3.3 Statistical Results of Stability Trial

A plot of phenobarbital with a target concentration of 10,000,000 ng/mL against time showed that all samples were above 90% of the target concentration (Figure 2). Homogeneity of the chemical concentration within the testing container was evaluated at time 0. Because one sample from the bottom section was in the same range as concentrations from the top section, a statistical difference was not detected. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of phenobarbital was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 13 weeks (Table 3). Thus, this stock solution was considered stable for the required 12-week testing/holding period. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses based on target concentrations ranged from 94% to 103%. The complete analysis is presented in Appendix E.

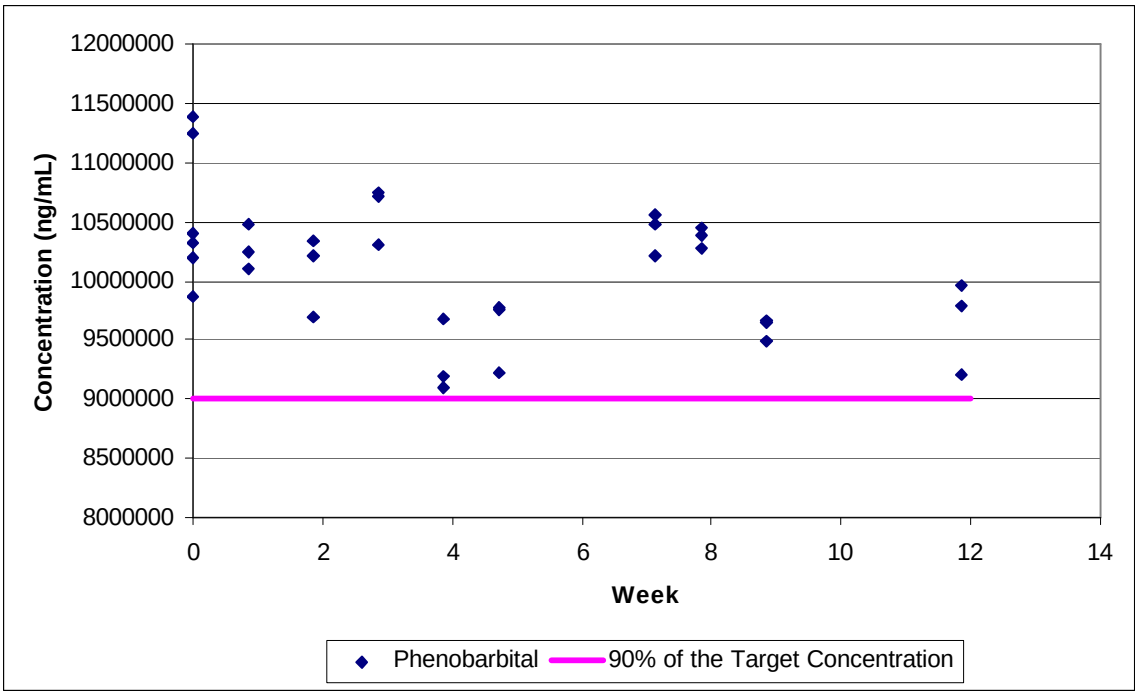


Figure 2. Observed Concentration of Phenobarbital with a Target Concentration of 10,000,000 ng/mL Against Time

Table 3. Summary of Statistical Results for Phenobarbital

WA-2-14-02 Statistical Analysis conducted by Valerie Cullinan Using Minitab Version 13.32, Minitab Inc., 1999.	1837-1-2 Phenobarbital
Target Concentration (ng/mL)	10000000
Number of determinations	1
Number of weeks tested	12
Number of replicates per day	3
Number of outliers removed	0
Number of observations removed	0
Overall Mean Concentration	10094590
95% Upper CL	10256605
error degrees of freedom	32
1-sample t-test of Ho: m >= Target	NS [a]
estimated intercept of ln(concentration) against time	16.1530
estimated slope of ln(concentration) against time	-0.0058
standard error of slope	0.0023
error degrees of freedom	31
Significance test of lack-of-fit for final model	S [b]
Significance test of Ho: b = 0 vs. H1: b ? 0	S
Lower 95% CL	-0.011
Upper 95% CL	-0.001
Maximum Percent Loss (using LCL)	8.1%
Mean Percent Loss (using bhat)	4.5%
LN(90% of Target)	16.0127
Number of weeks until at 90% of Target (using LCL)	13
Conclusion:	**Stable for 12 wks**

[a]Not Significant at a = 0.05

[b]Significant at a = 0.05

4.0 CONCLUSIONS

The phenobarbital stock used was determined to be 99.1% pure based on HPLC analyses at Battelle-Sequim; a certificate of purity was not available from the manufacturer. Stability testing of phenobarbital in Mazola corn oil concluded that the chemical was stable at the 10 mg/mL concentration for the required testing/holding period of 12 weeks.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 94% to 103%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

Certificate of Purity not Available from Manufacturer

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Phenobarbital

Chemical Name: Phenobarbital (MSL CF Login 1837), CMS 172554

CAS Number: 50-6-6

Lot Number: Lot 81K2620 - stored refrigerated in Bldg5 Rm 219

Expiration date: 6/2006

Manufacturer's Purity Information: not available

Manufacturer's Stability Information: stable

MSL Purity Results:
Purity (%) To be determined at MSL by LC or UV-VIS scan

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Phenobarbital

CAS: 50-06-6

Carrier(s): suspended in Mazola corn oil

Concentrations/Dilution Series: 10 mg/mL

In vitro or in *vivo tests*?: *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Testing/holding duration: 12 weeks

Design of Stability Test: One concentration of Phenobarbital, 10 mg/mL in Mazola corn oil, will be tested. The chemical will be sieved through an 80 mesh screen and material that passes will be suspended in Mazola corn oil with a magnetic stirrer. Samples of the suspension will be taken with a gavage needle, while the suspension is being vigorously stirred, at mid-depth in a 250 mL amber glass bottle, except for the first sampling, which will be sampled at 25% and 75% depth in triplicate to demonstrate homogeneity. The suspension will be stored in glass at 4 deg. C in the dark for 12 weeks, sampled at 8 times in triplicate and analyzed monthly by UV-VIS.

Number of replicates: 3

Duration: 12 weeks, sampling at 8 time points with triplicate samples taken each time

Other factors:
Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other: None

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:
Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
  - Chemical repository confirmatory test results of chemical identity and purity;
  - Chemical repository test results of lot-to-lot variation in chemical purity;
  - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- Dilution factor(s).

Prepare by Eric Crecelius

Distribution;
Tim Fortman
Deborah Coffee
Val Cullinan
Whitney Hansen

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C.1. Phenobarbital concentration in Mazola Corn Oil (ng/mL)

Target Conc.	Sample Name	Date	Phenobarbital (ng/mL)	Average	RSD	Recovery[1]
10000000 ng/ml	1837-1-2-1 Top R-1	10/16/02	9871823			
10000000 ng/ml	1837-1-2-1 Top R-2	10/16/02	10405445	10159422	2.65%	102%
10000000 ng/ml	1837-1-2-1 Top R-3	10/16/02	10200998			
10000000 ng/ml	1837-1-2-1 Bott R-1	10/16/02	10317041			
10000000 ng/ml	1837-1-2-1 Bott R-2	10/16/02	11244260	10984072	5.30%	110%
10000000 ng/ml	1837-1-2-1 Bott R-3	10/16/02	11390916			
blank	1837 Pheno Blnk 1	10/16/02	250000 U			
10000000 ng/ml	1837-1-2-2 R-1	10/22/02	10473674			
10000000 ng/ml	1837-1-2-2 R-2	10/22/02	10107970	10276501	1.80%	103%
10000000 ng/ml	1837-1-2-2 R-3	10/22/02	10247858			
blank	1837 Pheno Blnk 2	10/22/02	250000 U			
10000000 ng/ml	1837-1-2-3 R-1	10/29/02	9698422			
10000000 ng/ml	1837-1-2-3 R-2	10/29/02	10215889	10084350	3.37%	101%
10000000 ng/ml	1837-1-2-3 R-3	10/29/02	10338738			
blank	1837 Pheno Blnk 3	10/29/02	250000 U			
10000000 ng/ml	1837-1-2-4 R-1	11/05/02	10309549			
10000000 ng/ml	1837-1-2-4 R-2	11/05/02	10706868	10587165	2.28%	106%
10000000 ng/ml	1837-1-2-4 R-3	11/05/02	10745078			
blank	1837 Pheno Blnk 4	11/05/02	250000 U			
10000000 ng/ml	1837-1-2-5 R-1	11/12/02	9679601			
10000000 ng/ml	1837-1-2-5 R-2	11/12/02	9198365	9323160	3.36%	93.2%
10000000 ng/ml	1837-1-2-5 R-3	11/12/02	9091514			
blank	1837 Pheno Blnk 5	11/12/02	250000 U			
10000000 ng/ml	1837-1-2-6 R-1	11/18/02	9218319			
10000000 ng/ml	1837-1-2-6 R-2	11/18/02	9779975	9585813	3.32%	95.9%
10000000 ng/ml	1837-1-2-6 R-3	11/18/02	9759146			
blank	1837 Pheno Blnk 6	11/18/02	250000 U			
10000000 ng/ml	1837-1-2-7 R-1	12/05/02	10209633			
10000000 ng/ml	1837-1-2-7 R-2	12/05/02	10479046	10414561	1.74%	104%
10000000 ng/ml	1837-1-2-7 R-3	12/05/02	10555004			
blank	1837 Pheno Blnk 7	12/05/02	250000 U			
10000000 ng/ml	1837-1-2-8 R-1	12/10/02	10277012			
10000000 ng/ml	1837-1-2-8 R-2	12/10/02	10386122	10369912	0.83%	104%
10000000 ng/ml	1837-1-2-8 R-3	12/10/02	10446602			
blank	1837 Pheno Blnk 8	12/10/02	250000 U			
10000000 ng/ml	1837-1-2-9 R-1	12/17/02	9496789			
10000000 ng/ml	1837-1-2-9 R-2	12/17/02	9663303	9601503	0.95%	96.0%
10000000 ng/ml	1837-1-2-9 R-3	12/17/02	9644418			
blank	1837 Pheno Blnk 9	12/17/02	250000 U			
10000000 ng/ml	1837-1-2-10 R-1	01/07/03	9214545			
10000000 ng/ml	1837-1-2-10 R-2	01/07/03	9789508	9654036	4.04%	96.5%
10000000 ng/ml	1837-1-2-10 R-3	01/07/03	9958054			
blank	1837 Pheno Blnk 10	01/07/02	250000 U			

[1] Recovery is relative to the target concentration
U = Not detected at a value greater than the MDL

Table C.2. CCV Data for Phenobarbital Concentration in Mazola Corn Oil

Sample Name	Phenobarbital (ng/mL)	Recoveries
Phen200PP-1189C CCV	213.2	107%
Phen 200 PP-1189C	216.1	108%
Phen500PP-1189B CCV	529.7	106%
Phen 500 PP-1189B	521.1	104%
Phen200PP-1189C CCV	220.2	110%
Phen 200 PP-1189C	211.2	106%
Phen500PP-1189B CCV	523.1	105%
Phen 500 PP-1189B	511.1	102%
Phen500PP-1189B CCV	489.3	97.9%
Phen 500 PP-1189C	513.1	103%
Phen500PP-1189B CCV	526.0	105%
Phen 500 PP-1189B	436.9	87.4%
Phen500PP-1189B CCV	499.4	99.9%
Phen500PP-1189B CCV	493.9	98.8%
Phen500PP-1189B CCV	476.0	95.2%
Phen500PP-1189B CCV	491.1	98.2%
Phen500PP-1189B CCV	485.2	97.0%
Phen500PP-1189B CCV	492.3	98.5%
Phen500PP-1189B CCV	500.7	100%
Phen500PP-1189B CCV	497.0	99.4%
Phen500PP-1189B CCV	532.3	106%
Phen500PP-1189B CCV	457.7	91.5%

Table C.3. Internal Standards Data for Phenobarbital in Mazola Corn Oil

Sample Name	Date	5A Androstane Recovery
Not applicable		

Table C.4. Peroxide Concentration in Mazola Corn Oil (meq/kg)

Sample	Analysis Date	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	09/05/02	0.5	0.005	5.00	0.50		
Mazola Corn Oil Expiration 6-03 R-1	09/05/02	1.9	0.005	5.01	1.90		
Mazola Corn Oil Expiration 6-03 R-2	09/05/02	1.8	0.005	5.36	1.68	1.77	6.41
Mazola Corn Oil Expiration 6-03 R-3	09/05/02	1.8	0.005	5.16	1.74		
Mazola Corn Oil Expiration 1-04 R-1	09/05/02	1.2	0.005	4.92	1.22		
Mazola Corn Oil Expiration 1-04 R-2	09/05/02	1.5	0.005	5.2	1.44	1.34	8.31
Mazola Corn Oil Expiration 1-04 R-3	09/05/02	1.4	0.005	5.13	1.36		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-02
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.
———— 6/4/2003 11:16:50 AM ————————————————

Results for: Week 0

Two-Sample T-Test and CI: Phenobarbital, section

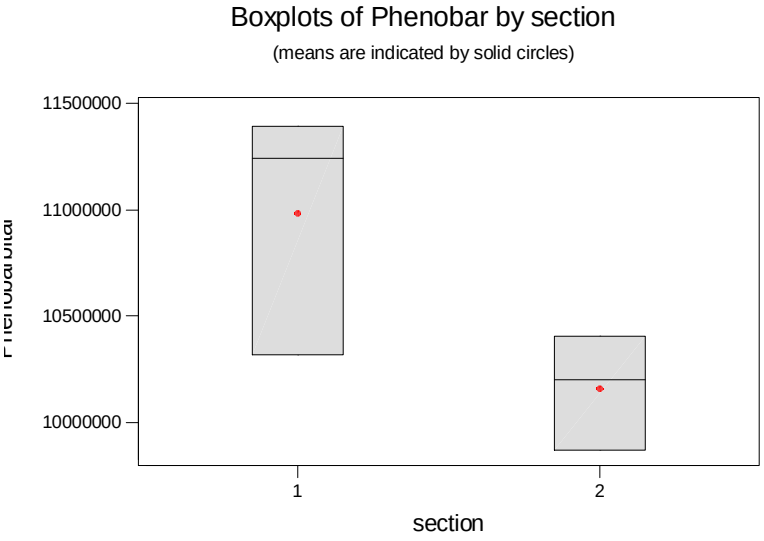
1 = bottom
2 = top

```
Two-sample T for Phenobarbital

section     N      Mean     StDev   SE Mean
1           3  10984072    582302    336192
2           3  10159422    269230    155440

Difference = mu (1) - mu (2)
Estimate for difference:  824650
95% CI for difference: (-768996, 2418297)
T-Test of difference = 0 (vs not =): T-Value = 2.23  P-Value = 0.156  DF = 2
```

Very poor power!

NS

Boxplots of Phenobarbital by section



Kruskal-Wallis Test: Phenobarbital versus section

```
Kruskal-Wallis Test on Phenobarbital

section     N    Median    Ave Rank         Z
1           3  11244260         4.7      1.53
2           3  10200998         2.3     -1.53
Overall     6                   3.5

H = 2.33  DF = 1  P = 0.127

* NOTE * One or more small samples
```

Conclusion: For the week 0 data, the test between sections has very poor power, note the width of the 95% CI of the difference (-768996, 2418297). Because one

sample from the bottom section was in the same range as concentrations from the top section, no difference could be detected.

Results for: Stability Data

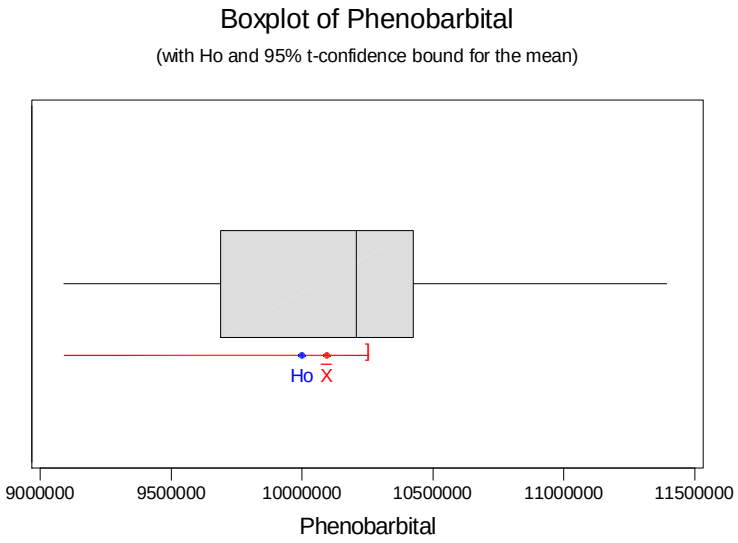
- Performs a one-sample t-test for mu less than TARGET &

```
What is the target value for X    3
DATA> 10000000
```

One-Sample T: Phenobarbital

```
Test of mu = 10000000 vs mu < 10000000

Variable          N      Mean     StDev   SE Mean
Phenobarbital     33  10094590    549446     95646

Variable      95.0% Upper Bound        T      P
Phenobarbita           10256605     0.99  0.835      NS
```

t Boxplot of Phenobarbital




```
Outliers are < Median-3*IQD OR > Median+3*IQD

Boundary for outliers are values <     7998597  and >     12420669

No outliers
```

- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	16.1052
0	2	16.1578
0	3	16.1380
0	1	16.1493
0	2	16.2354
0	3	16.2483
1	1	16.1644
1	2	16.1288
1	3	16.1426
2	1	16.0875
2	2	16.1395
2	3	16.1514
3	1	16.1486
3	2	16.1864
3	3	16.1900
4	1	16.0855
4	2	16.0345
4	3	16.0229
5	1	16.0367
5	2	16.0958
5	3	16.0937
7	1	16.1388
7	2	16.1649
7	3	16.1721
8	1	16.1454
8	2	16.1560
8	3	16.1618
9	1	16.0665
9	2	16.0838
9	3	16.0819
12	1	16.0363
12	2	16.0968
12	3	16.1139

- Conducts Simple Linear Regression

Regression Analysis: Phenobarbital versus Week

The regression equation is
Phenobarbital = 16.2 - 0.00581 Week

Predictor	Coef	SE Coef	T	P	
Constant	16.1530	0.0139	1161.92	0.000	
Week	-0.005811	0.002326	-2.50	0.018	*

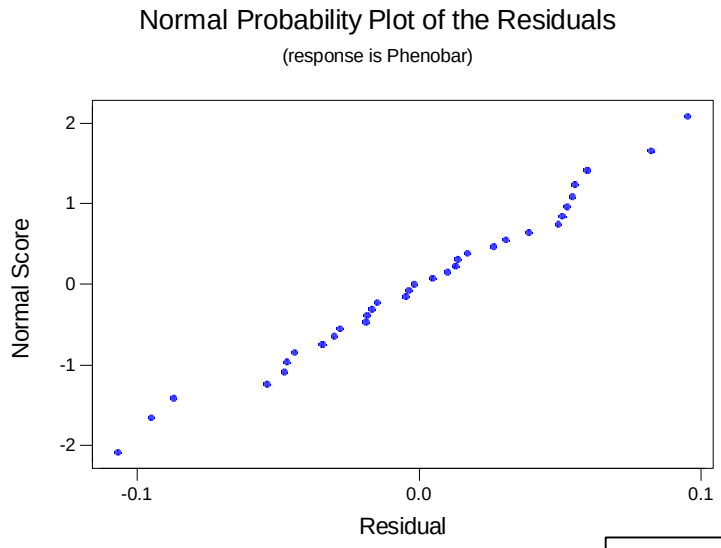
S = 0.05040 R-Sq = 16.8% R-Sq(adj) = 14.1%

Analysis of Variance

Source	DF	SS	MS	F	P	
Regression	1	0.015859	0.015859	6.24	0.018	
Residual Error	31	0.078755	0.002540			
Lack of Fit	8	0.049845	0.006231	4.96	0.001	**
Pure Error	23	0.028910	0.001257			
Total	32	0.094614				

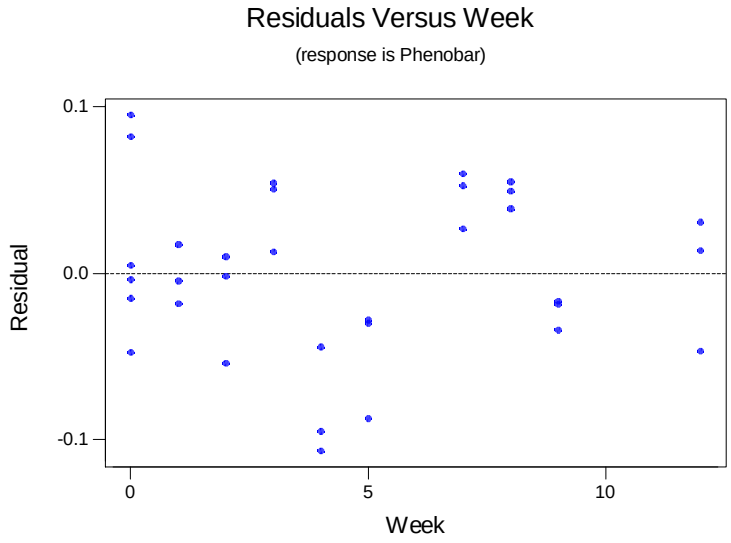
```
Unusual Observations
Obs       Week    Phenobar         Fit      SE Fit    Residual    St Resid
 18        4.0     16.0229     16.1298      0.0089     -0.1069       -2.16R

R denotes an observation with a large standardized residual
```

Normplot of Residuals for Phenobar



High and low residuals balance out each other, no data will be removed.

Residuals from Phenobarbital vs Week




```
Do you want to remove any data points? (yes OR no)
n

Should a quadratic be fit? (yes OR no)
n
```

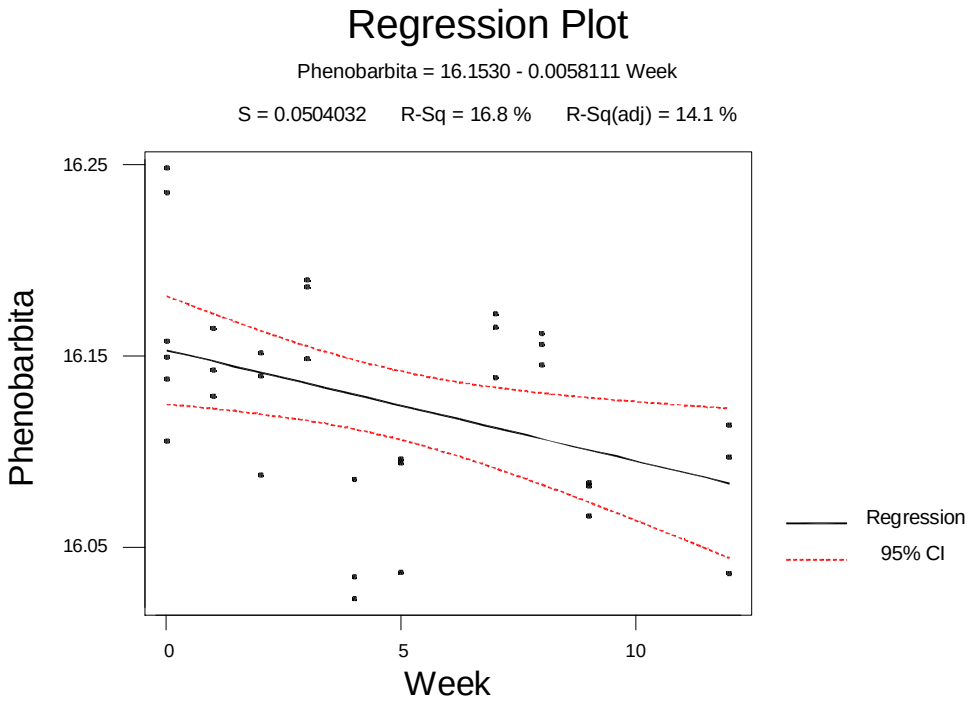
- Power analysis for t-test of slope less than zero

Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0504032

Sample
  Size   Power  Difference
    31  0.9900     -0.0368
```

- That means we would detect a mean of 16.081 as significantly less than ln(10000000) = 16.118 or a change of 9638689 from 10000000 = 3.6% loss.

- Fit 95% confidence bands about the fitted simple linear model



- **Conclusion – all data points were greater than 90% of the target concentration of 10,000,000 ng/mL. The slope through time was significant and the concentration was expected to stay above 90% of the target concentration for an estimated 13 weeks. Thus, the chemical is stable for the required 12 week testing period.**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Phenobarbital in-life test suspension samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Phenobarbital in corn oil

TEST SOLUTION, SAMPLE CUSTODY, AND PROCESSING:

Test suspension samples were prepared by the EDSP Chemical Repository, Sequim, WA, using phenobarbital (CF 1837, Sigma lot # 81K2620, expiration date 06/06) dissolved in Mazola corn oil (corn oil was from containers with the following expiration dates: 6/12/03, 1/1/04, and 4/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time. Three test suspensions at each of the test concentrations were prepared at one time on 01/22/03 and shipped on two different dates, 01/23/03 (Rep 1) and 01/27/03 (Reps 2 and 3). Samples were prepared at two test concentrations: 10 mg/mL and 20 mg/mL. The 10 mg/mL concentration was prepared by adding 2.0 g of phenobarbital in 184 g of corn oil in a pre-cleaned, amber glass container. The 20 mg/mL concentration was prepared by adding 4.0 g of phenobarbital in 182 g of corn oil. Phenobarbital was sieved through an 80-mesh, stainless-steel screen prior to weighing. Stir bars were added to keep the chemical in suspension. The samples were analyzed on 01/23/03 to verify concentrations prior to shipping (Table 1).

The test suspension was sampled five times during the male test (1/26/03, 2/2/03, 2/9/03, 2/16/03, 2/23/03). Data are reported in Table 2. Table 3 provides results of analysis of remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test.

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:

The container was placed on a magnetic stir plate and stirred. 1-mL triplicate samples were removed and each placed in a tared, 60 mL, amber glass bottle. The weight of the sample was determined gravimetrically. 50 mL of acetonitrile (ACN) was added and the bottle agitated to mix. For the 10 mg/mL concentration, 0.01 mL was transferred to an auto sampler vial with 0.99 mL of 60% ACN in water. For the 20 mg/mL concentration, 0.005 mL was transferred to an auto sampler vial with 0.995 mL of 60% ACN in water.

In-life and Returned Container Samples:

For the containers with sufficient material to analyze, the samples of remaining dosing solution were removed from the refrigerator, allowed to warm to room temperature, and then stirred using a magnetic stir bar and stir plate. About 1 mL was sampled and placed in a tared, 60 mL, amber glass bottle. The weight of the sample was determined gravimetrically. 50 mL of acetonitrile (ACN, JT Baker lot # Y02820) was added and the bottle agitated to mix. Then,

0.01 was transferred to a 1.8-mL vial with 0.99 mL of 60% ACN:Water. This solution was then transferred to a high performance liquid chromatograph (HPLC) auto sampler vial for analysis.

The in-life samples were returned in 20 mL scintillation vials, which contained a slurry with the phenobarbital settled to the bottom. The entire sample was extracted to ensure accurate analysis. The vial was weighed and the contents poured into 120 mL, amber-glass bottle. 100 mL of ACN was used for these samples. The scintillation vial was rinsed with part of the 100 mL ACN. This rinse was then poured into the amber vial and the rinsing repeated to ensure complete transfer of the sample. The empty vial was dried and re-weighed. The amber bottles were agitated to mix, and 0.005 mL transferred to an auto sampler vial with 0.995 mL ACN:water. This was transferred to an HPLC vial for analysis.

SAMPLE ANALYSIS: The samples were analyzed using an HPLC with an ultraviolet/visible (UV/VIS) detector at the 225-nm wavelength. A 60:40% ACN:water (v:v) mix was used as the eluent at 1.5 mL/minute. Separation was attained using a Supelco (25 cm x 4.8 mm) C-18 column for the samples analyzed on 1/23/03 and a Phenominex Synergi (25 cm X 4.8 mm, C-18 column) for all remaining samples. Calibration with a five-point curve was conducted using calibration standard PP-1189, A-E. For samples analyzed using the HPLC system, data are stored in MSL5, Room 219, on the computer with a property number of WV04738.

Data Quality Objectives	**Control Limits**
Procedural Blank	<5 X MDL
Blank Spike Recovery	40% – 120%
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: HPLC with a UV/VIS detector at the 225-nm wavelength.

CALIBRATION: Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1189, A-E (curve from 10/17/02) for the initial test solutions and calibration standard PP-1189d (curve from 5/30/03) for the in-life and remainder samples, with a continuing calibration verification (CCV) sample analyzed every 10 samples.

CONTINUING STANDARD RECOVERY: Percent recovery results for two initial and CCV samples analyzed with the in-life sample data set ranged from 92% to 106%, with a mean recovery of 100%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK: Phenobarbital was not detected above the detection limit in the three blanks analyzed with the test solution and in-life samples.

DETECTION LIMIT: The phenobarbital detection limit was 250 mg/L, determined by analysis of the low concentration standard (50 µg/L) and the dilution factor of 5,000 that used for the unknowns (MDL = 5,000 * 50 µg/L). No data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed. In this analysis, sampling was performed by taking the sample material from flask through to analysis. Analyzing a spiked sample would be no different from analyzing a CCV.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSD) for the two test solutions prepared and shipped were 1.0% for the 10-mg/mL replicates and 5.6% for the 20-mg/mL replicates.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of Formulation Concentrations Prepared on 1/22/03 and Analyzed on 1/23/03

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	% RSD
Corn oil blank	RTI-Blank-1	0.250U		
10 mg/mL	2-14 H-M R-1	9.55		
10 mg/mL	2-14 H-M R-2	9.64	9.64	1.0
10 mg/mL	2-14 H-M R-3	9.74		
20 mg/mL	2-14 I-M R-1	18.2		
20 mg/mL	2-14 I-M R-2	18.6	19.0	5.6
20 mg/mL	2-14 I-M R-3	20.2		

Table 2. Phenobarbital In-life Sample Concentrations - Males

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
01/26/03	03/05/03	05/30/03	10 mg/mL	1-26-03 H-M	9.40	94%
02/02/03	03/05/03	05/30/03	10 mg/mL	2-2-03 H-M	9.77	98%
02/09/03	03/05/03	05/30/03	10 mg/mL	2-9-03 H-M	9.92	99%
02/16/03	03/05/03	05/30/03	10 mg/mL	2-16-03 H-M	10.2	102%
02/23/03	03/05/03	05/30/03	10 mg/mL	2-23-03 H-M	10.3	103%
01/26/03	03/05/03	05/30/03	20 mg/mL	1-26-03 I-M	19.9	100%
02/02/03	03/05/03	05/30/03	20 mg/mL	2-2-03 I-M	20.5	103%
02/09/03	03/05/03	05/30/03	20 mg/mL	2-9-03 I-M	19.6	98%
02/16/03	03/05/03	05/30/03	20 mg/mL	2-16-03 I-M	19.7	99%
02/23/03	03/05/03	05/30/03	20 mg/mL	2-23-03 I-M	19.8	99%

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Propylthiouracil in Mazola Corn Oil

November 3, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory
1529 West Sequim Bay Road
Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology
Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Propylthiouracil in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Propylthiouracil in Mazola Corn Oil

Parameter	Chemical
Compound Name	Propylthiouracil
CAS #	51-52-5
Central File No.	CF-1823
Initial Receipt Date	10/18/01
Expiration Date	Oct-04
Manufacturer	TCI America
Lot Number	GB01
Battelle Study #	WA2-14-02-02
Method	SW 846, 9065 Modified

Executive Summary

The chemical purity of propylthiouracil determined by the manufacturer was 99.6%. The purity result from Battelle-Sequim using gravimetric analysis was determined to be 99.9%. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of propylthiouracil was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 8 weeks. Thus, stability testing of the propylthiouracil stock solution in Mazola corn oil was not considered stable at 0.4 mg/mL for the entire required testing and holding period of 12 weeks.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/02 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 74% to 108%. Recoveries of post-test formulation samples returned to Battelle from RTI based on target concentrations ranged from 94% to 124%..

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA2-14-02-02, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of propylthiouracil (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_propylthiouracil-cornoil.doc, PSTP_WA-2-14_ propylthiouracil-cornoil.doc, DSUM_WA2-14_Propylthiouracil-crnoil.xls, and DAF_WA-2-14_Propylthiouracil-cornoil.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, propylthiouracil, (CAS No. 51-52-5) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Propylthiouracil was purchased from TCI America and lot number GB01 was initially received on 10/18/01 with an expiration date of Oct-04 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1823) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Mazola corn oil with expiration dates of 6/03 and 1/04 was purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-02

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Propylthiouracil (MSL CF 1823)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 0.4 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Testing/holding duration: 12 weeks

Chemical Information

Chemical Name: Propylthiouracil

CAS: 51-52-5

Any known purity information: may refer to attached documentation
Manufacturer's Purity Information: 99.6% pure
Any known stability information: may refer to attached documentation
Manufacturer's Stability Information: stable
Desired purity (%) for test? 95% or greater

Figure 1. EDSP Requisition Form for Propylthiouracil

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Propylthiouracil
CAS #	51-52-5
Central File No.	CF-1823
Initial Receipt Date	10/18/01
Expiration Date	Oct-04
Manufacturer	TCI America
Lot Number	GB01
Manufacturer's Purity	99.6%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA2-14-02-02
Method	SW 846, 9065 Modified

2.2 Chemical Purity

Chemical purity was verified by a gravimetric method and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted by creating a solution of propylthiouracil by adding 0.4998 g propylthiouracil to a 25 mL volumetric flask. A 0.5 mL aliquot of 50% sodium hydroxide (NaOH) was then added to the flask which was then diluted to the 25 mL mark with deionized water. To perform the analysis, 5 mL of the solution was pushed through a 0.2 um syringe filter followed by 10 mL of deionized water. Then the filter was dried by blowing helium through the filter for about 10 minutes. Syringe filters were then stored in a dessicator for 12 hours and weighed. The percent purity was determined by comparing a blank with the filtered material and the remainder was considered impurities. Three replicates were analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. A stock solution was prepared to arrive at the chemical concentration requested for stability analysis (Table 2). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

A propylthiouracil stock matrix was prepared on 10/14/02 for testing as described in Table 2. Briefly, for the 0.4 mg/mL propylthiouracil concentration, 0.080 g was weighed into a 250 mL wide-mouth amber glass bottle, 186 g of Mazola corn oil was added, the sample was stirred, and stored in a refrigerator at 4ºC ± 2ºC during the duration of the study..

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA2-14-02-02 12 Weeks	Propylthiouracil	0.4 mg/mL	1823-1b-2	0.080 g Propylthiouracil in 186 g Mazola corn oil

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by ultra violet (UV) absorption analysis. Triplicate aliquots were tested for the 0.4 mg/mL concentration. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

The propylthiouracil stock solution was sampled by removing it from the refrigerator, allowing it to warm to room temperature, stirring it overnight, removing triplicate 1 mL samples, and placing them in a tared 30 mL amber bottle. At the beginning of the stability trial (10/16/02), vertical homogeneity was assessed by removing samples from the top (about 0.25 inches below the surface) and bottom (about 1 inch from the bottom). Subsequent samples were removed from the center of the sample container. After samples were collected, the actual weight was determined gravimetrically, then 25 mL NaOH in deionized water was added. The alkaline water was prepared from 0.6 mL of a 50% by weight NaOH in water diluted to 1 L. The container was agitated for about two minutes to mix. After addition of NaOH, 3 mL of solution was transferred to a syringe with a Gelman acrodisk CR, PFTE 0.2 um filter attached. The filtered solution was placed into a 2 mL auto sampler vial, and about 0.5 mL removed and placed into a 5 mL cuvette that works with the Beckman DU8 spectrophotometer. A total of 1.5 mL of the alkaline water solution was added to the sample, the cuvette was swirled to mix, and the sample was analyzed using the Beckman DU8 spectrophotometer at the 260 nm wavelength with a slit width of 0.5 and the average read time set to 3. The unknown absorption was compared to that of the calibration standards.

Calibration was done using dilutions prepared from standard PP-1188 until 11/12/02 when a new standard, PP-1197 was used. Initial and continuing calibration verification (ICV and CCV, respectively) were analyzed at the beginning and end of every run. At least a 4 –point calibration series was analyzed with each sample run. PP-1188 was a serial dilution of PP-1187 which was made by weighing 0.1011 grams of propylthiouracil into a 100 mL volumetric flask. This was then diluted to the 100 mL mark with alkaline water. The PP-1188 series (A through E) was made using the following amounts of PP-1187 which was then diluted to the 100 mL mark with the alkaline water: PP-1188A was 2 mL PP-1187; B was 1 mL PP-1187; PP-1188C was 0.5 mL PP-1187; PP-1188D was 0.1 mL PP-1187; and PP-1188E was 0.05 mL PP-1187. PP-1197 series was made in the same way except that 0.1000 grams of propylthiouracil was used.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fit to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim determined purity of the propylthiouracil using a gravimetric method. The purity was determined by dissolving an aliquot of the propylthiouracil and determining the insoluble fraction. This fraction (considered the impurity), was then used to determine the purity. This method yielded a purity of 99.9%. Chemical purity of propylthiouracil determined by the manufacturer was 99.6% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 10/16/02. Chemical concentrations were determined 10 times between 10/16/02 and 01/07/03. The analytical and quality control (QC) results are presented in Appendix C. A single preparation blank was analyzed with every sample for QC purposes. Because Mazola corn oil in the solution contributed to the absorbance at the wavelength used, the blanks produced an apparent propylthiouracil value at concentrations ranging from 39.8 U to 159 µg/mL . Stability sample concentrations were blank corrected. CCV results ranged from 94.4% to 111%. Internal standards were not analyzed. The MDL was 50.6 µg/mL. The dilution factor of the formulation can be taken into account, and thus, the MDL of the diluted sample was 0.5 µg/mL.

Mazola corn oil with expiration dates of 6/03 and 1/04 were purchased from local grocery stores and used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentrations were measured on 9/05/2002 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn oil was 1.77 meq/kg and 1.34 meq/kg for samples expiring on 6/03 and 1/04, respectively. This level of peroxide was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

3.3 Statistical Results of Stability Trial

A plot of propylthiouracil with a target concentration of 400 µg/mL against time showed a potential decay in concentration (Figure 2). Homogeneity of the chemical concentration within the testing container was evaluated at time 0. Because one sample from both the top and bottom sections was approximately the same concentration, no difference was detected. All but three stability samples were above 90% of the target value. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of propylthiouracil was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 8 weeks (Table 3). Because of the significant slope ($p = 0.002$), this stock solution was considered stable for only 8 of the required 12-week testing/holding period. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

In-life chemistry recoveries for all doses based on target concentrations ranged from 74% to 108%. Recoveries of post-test formulation samples returned to Battelle from RTI based on target concentrations ranged from 94% to 124%. The complete analysis is presented in Appendix E.

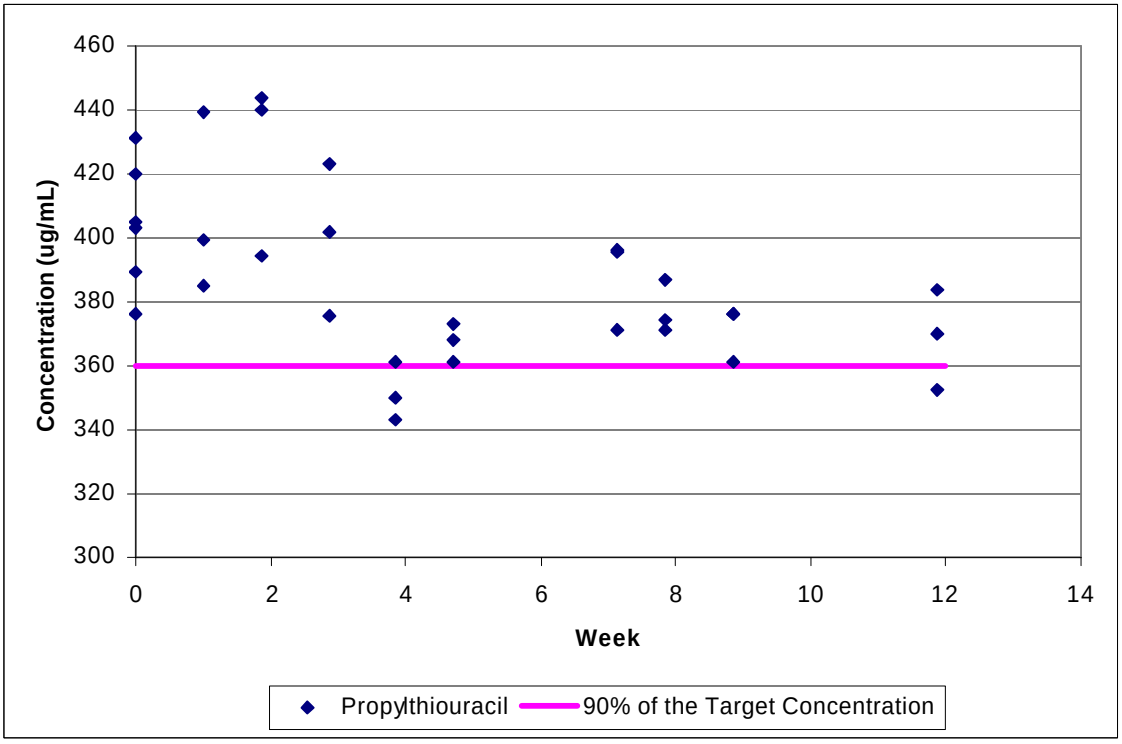


Figure 2. Observed Concentration of Propylthiouracil with a Target Concentration of 400 mg/mL Against Time

Table 3. Summary of Statistical Results for Propylthiouracil

WA-2-14-02 **Statistical Analysis conducted by Valerie Cullinan** **Using Minitab Version 13.32, Minitab Inc., 1999.**	**1823-1b-2** **Propylthiouracil**
Target Concentration (ug/mL)	400
Number of determinations	1
Number of weeks tested	12
Number of replicates per day	3
Number of outliers removed	0
Number of observations removed	0
Overall Mean Concentration	388
95% Upper CL	396
error degrees of freedom	32
1-sample t-test of Ho: μ >= Target	S [a]
estimated intercept of ln(concentration) against time	6.0016
estimated slope of ln(concentration) against time	-0.0093
standard error of slope	0.0027
error degrees of freedom	31
Significance test of lack-of-fit for final model	S
Significance test of Ho: β = 0 vs. H1: β ? 0	S
Lower 95% CL	-0.015
Upper 95% CL	-0.004
Maximum Percent Loss (using LCL)	11.2%
Mean Percent Loss (using bhat)	7.2%
LN(90% of Target)	5.8861
Number of weeks until at 90% of Target (using LCL)	8
Conclusion:	**Stable for 8 wks**

[a]Significant at a = 0.05

4.0 CONCLUSIONS

The stated chemical purity by the manufacturer was 99.6%. Battelle-Sequim laboratory analyses determined the purity to be 99.9%. Stability testing of propylthiouracil in Mazola corn oil concluded that the chemical was stable at the 0.4 mg/mL concentration for a period of 8 weeks. Thus, the propylthiouracil stock solution in Mazola corn oil was not considered stable at 0.4 mg/mL for the required testing/holding period of 12 weeks.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

In-life chemistry recoveries for all doses based on target concentrations ranged from 74% to 108%. Recoveries of post-test formulation samples returned to Battelle from RTI based on target concentrations ranged from 94% to 124%.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

TCI AMERICA

CERTIFICATE OF ANALYSIS

P0533
Lot# GB01
CAS# 51-52-5

6-N-PROPYL-2-THIOURACIL

Appearance:	White powder
Solubility(in 1N NaOH, 1/20):	Clear
Assay(tit.):	99.6%

9211N. Harborgate St. Portland, OR 97203 Phone: (503)283-1681 (800)423-8616 Fax: (503)283-1987

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Propylthiouracil

Chemical Name: Propylthiouracil (MSL CF 1823), CMS 173694

CAS Number: 51-52-5

Lot Number: GB01 , stored at RT in MSL5, Rm 219

Expiration date: 10/2004

Manufacturer's Purity Information: 99.6%

Manufacturer's Stability Information: stable

MSL Purity Results:
Purity (%) To be determined at MSL by gravimetric analysis

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Propylthiouracil

CAS: 51-52-5

Carrier(s): suspended in Mazola corn oil

Concentrations/Dilution Series: 0.4 mg/mL

In vitro or in *vivo tests*? *In vivo*

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Testing/holding duration: 12 weeks

Design of Stability Test: One concentration of Propylthiouracil, 0.4 mg/mL in Mazola corn oil, will be tested. The chemical will be sieved through an 80 mesh screen and material that passes will be suspended in Mazola corn oil with a magnetic stirrer. Samples of the suspension will be taken with a gavage needle, while the suspension is being vigorously stirred, at mid-depth in a 250 mL amber glass bottle, except for the first sampling, which will be sampled at 25% and 75% depth in triplicate to demonstrate homogeneity. The suspension will be stored in glass at 4 deg. C in the dark for 12 weeks, sampled at least 8 times in triplicate and analyzed monthly by UV-VIS.

Number of replicates: 3

Duration: 12 weeks, sampling at least 8 time points with triplicate samples taken each time

Other factors:
Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other: None

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:
Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
    - Chemical repository confirmatory test results of chemical identity and purity;
    - Chemical repository test results of lot-to-lot variation in chemical purity;
    - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- Dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C1. Propylthiouracil concentration in Mazola Corn Oil (µg/mL)

Target Concentration	Name	Date Analyzed	Propylthiouracil[a]	Average	RSD	Recovery[b]
400 µg/mL	1823-1b-2-1 Top R-1	10/16/2002	389			97.3%
400 µg/mL	1823-1b-2-1 Top R-2	10/16/2002	405	390	3.71%	101%
400 µg/mL	1823-1b-2-1 Top R-3	10/16/2002	376			94.0%
400 µg/mL	1823-1b-2-1 Bottom R-1	10/16/2002	403			101%
400 µg/mL	1823-1b-2-1 Bottom R-2	10/16/2002	420	418	3.41%	105%
400 µg/mL	1823-1b-2-1 Bottom R-3	10/16/2002	431			108%
400 µg/mL	1823-1b-2-2 R-1	10/23/2002	399			99.8%
400 µg/mL	1823-1b-2-2 R-2	10/23/2002	439	408	6.95%	110%
400 µg/mL	1823-1b-2-2 R-3	10/23/2002	385			96.2%
400 µg/mL	1823-1b-2-3 R-1	10/29/2002	440			110%
400 µg/mL	1823-1b-2-3 R-2	10/29/2002	394	426	6.51%	98.5%
400 µg/mL	1823-1b-2-3 R-3	10/29/2002	444			111%
400 µg/mL	1823-1b-2-4 R-1	11/5/2002	423			106%
400 µg/mL	1823-1b-2-4 R-2	11/5/2002	402	400	5.94%	100%
400 µg/mL	1823-1b-2-4 R-3	11/5/2002	376			94.0%
400 µg/mL	1823-1b-2-5 R-1	11/12/2002	350			87.5%
400 µg/mL	1823-1b-2-5 R-2	11/12/2002	343	351	2.60%	85.8%
400 µg/mL	1823-1b-2-5 R-3	11/12/2002	361			90.3%
400 µg/mL	1823-1b-2-6 R-1	11/18/2002	368			92.0%
400 µg/mL	1823-1b-2-6 R-2	11/18/2002	361	367	1.67%	90.3%
400 µg/mL	1823-1b-2-6 R-3	11/18/2002	373			93.3%
400 µg/mL	1823-1b-2-7 R-1	12/5/2002	396			99.1%
400 µg/mL	1823-1b-2-7 R-2	12/5/2002	396	388	3.67%	99.0%
400 µg/mL	1823-1b-2-7 R-3	12/5/2002	371			92.9%
400 µg/mL	1823-1b-2-8 R-1	12/10/2002	387			96.7%
400 µg/mL	1823-1b-2-8 R-2	12/10/2002	374	377	2.22%	93.5%
400 µg/mL	1823-1b-2-8 R-3	12/10/2002	371			92.8%
400 µg/mL	1823-1b-2-9 R-1	12/17/2002	376			94.0%
400 µg/mL	1823-1b-2-9 R-2	12/17/2002	376	371	2.28%	94.0%
400 µg/mL	1823-1b-2-9 R-3	12/17/2002	361			90.3%
400 µg/mL	1823-1b-2-10 R-1	1/7/2003	384			95.9%
400 µg/mL	1823-1b-2-10 R-2	1/7/2003	370	369	4.27%	92.5%
400 µg/mL	1823-1b-2-10 R-3	1/7/2003	352			88.1%

[a] Propylthiouracil values were blank corrected

[b] Recovery is relative to the target concentration

Table C1. Continued

Sample Name	Date Analyzed	Propylthiouracil (µg/mL)
1823-1b-2-1 Blank	10/16/02	65.1
1823-1b-2-2 Blank	10/23/02	110
1823-1b-2-2 Blank	10/23/02	106
1823-1b-2-2 Blank	10/23/02	96.4
1823-1b-2-3 Blank	10/29/02	117
1823-1b-2-3 Blank	10/29/02	108
1823-1b-2-3 Blank	10/29/02	130
1823-1b-2-4 Blank R-1	11/5/02	108
1823-1b-2-4 Blank R-2	11/5/02	83.7
1823-1b-2-4 Blank R-3	11/5/02	87.1
1823-1b-2-5 Blank R-1	11/12/02	64.0
1823-1b-2-5 Blank R-2	11/12/02	59.2
1823-1b-2-5 Blank R-3	11/12/02	76.1
1823-1b-2-6 Blank R-2	11/18/02	47.3
1823-1b-2-6 Blank R-3	11/18/02	55.1
1823-1b-2-6 Blank R-1	11/21/02	89.9
1823-1b-2-6 Blank R-2	11/21/02	59.1
1823-1b-2-6 Blank R-3	11/21/02	50.6 U
1823-1b-2-7 Blank R-1	12/5/02	159
1823-1b-2-7 Blank R-2	12/5/02	154
1823-1b-2-8 Blank R-1	12/10/02	50.9
1823-1b-2-8 Blank R-2	12/10/02	54.3
1823-1b-2-9 Blank R-1	12/17/02	50.6 U
1823-1b-2-9 Blank R-2	12/17/02	50.6 U
1823-1b-2-10 Blank R-1	1/7/03	51.2
1823-1b-2-10 Blank R-2	1/7/03	50.6 U
Corn oil blank 1g 0.5 ml/1.5ml	1/22/03	54.1
Corn oil blank 5g 0.1 ml/1.9ml	1/22/03	50.6 U
Corn oil blank 5g 0.05ml/2.95ml	1/22/03	50.6 U

U = Not detected at a value greater than the MDL

Table C.2. ICV and CCV Data for Propylthiouracil Concentration in Mazola Corn Oil

Sample Name	Date Analyzed	Propylthiouracil (µg/mL)	Recovery
ICV- 5.055 µg/mL	10/16/02	4.82	95.3%
CCV- 5.055 µg/mL	10/16/02	4.77	94.4%
ICV- 5.055 µg/mL	10/23/02	5.31	105%
CCV- 5.055 µg/mL	10/23/02	5.34	106%
ICV- 5.055 µg/mL	10/29/02	5.48	108%
CCV- 5.055 µg/mL	10/29/02	5.47	108%
CCV- 5.055 µg/mL	11/5/02	5.63	111%
CCV- 5.055 µg/mL	11/5/02	5.60	111%
ICV- 5.055 µg/mL	11/12/02	4.88	96.5%
CCV- 5.055 µg/mL	11/12/02	4.92	97.3%
ICV- 5.055 µg/mL	11/18/02	4.90	97.0%
CCV- 5.055 µg/mL	11/18/02	4.95	97.9%
ICV- 5.055 µg/mL	12/5/02	4.93	97.5%
CCV- 5.055 µg/mL	12/5/02	4.96	98.1%
ICV- 5.055 µg/mL	12/10/02	4.92	97.3%
CCV- 5.055 µg/mL	12/10/02	4.91	97.1%
ICV- 5.055 µg/mL	12/17/02	4.96	98.1%
CCV- 5.055 µg/mL	12/17/02	4.92	97.4%
ICV- 5.055 µg/mL	1/7/03	5.01	99.1%
CCV- 5.055 µg/mL	1/7/03	5.00	98.9%
	Test solution verification		
ICV- 5.055 µg/mL	11/21/02	4.93	97.5%
CCV- 5.055 µg/mL	11/21/02	4.91	97.1%

Table C.3. Internal Standards Data for Propylthiouracil in Mazola Corn Oil

Sample Name	Date	5A Androstane Recovery
Not applicable		

Table C.4. Peroxide Concentration in Mazola Corn Oil (meq/kg)

Sample	Analysis Date	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	09/05/02	0.5	0.005	5.00	0.50		
Mazola Corn Oil Expiration 6-03 R-1	09/05/02	1.9	0.005	5.01	1.90		
Mazola Corn Oil Expiration 6-03 R-2	09/05/02	1.8	0.005	5.36	1.68	1.77	6.41
Mazola Corn Oil Expiration 6-03 R-3	09/05/02	1.8	0.005	5.16	1.74		
Mazola Corn Oil Expiration 1-04 R-1	09/05/02	1.2	0.005	4.92	1.22		
Mazola Corn Oil Expiration 1-04 R-2	09/05/02	1.5	0.005	5.2	1.44	1.34	8.31
Mazola Corn Oil Expiration 1-04 R-3	09/05/02	1.4	0.005	5.13	1.36		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-02
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

5/31/2003 9:29:56 AM

Results for: Week 0

1 = bottom
2 = top

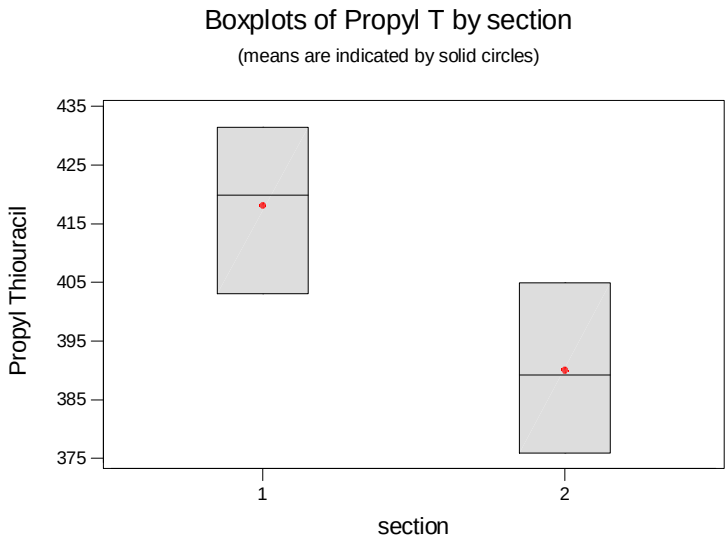
Two-Sample T-Test and CI: Propyl Thiouracil, section
Two-sample T for Propylthiouracil

section	N	Mean	StDev	SE Mean
1	3	418.1	14.3	8.2
2	3	390.0	14.5	8.4

Poor power!

Difference = mu (1) - mu (2)
Estimate for difference: 28.1
95% CI for difference: (-9.2, 65.4)
T-Test of difference = 0 (vs not =): T-Value = 2.40 P-Value = 0.096 DF = 3

NS



Kruskal-Wallis Test: Propylthiouracil versus section
Kruskal-Wallis Test on Propyl T

section	N	Median	Ave Rank	Z
1	3	419.9	4.7	1.53
2	3	389.2	2.3	-1.53
Overall	6		3.5	

H = 2.33 DF = 1 P = 0.127 NS

* NOTE * One or more small samples

Conclusion: For the week 0 data, the test between sections has poor power, note the width of the 95% CI of the difference (-9.2, 65.4). Because one sample from both the top and bottom sections was about the same concentration, no difference could be detected.

Results for: Stability Data

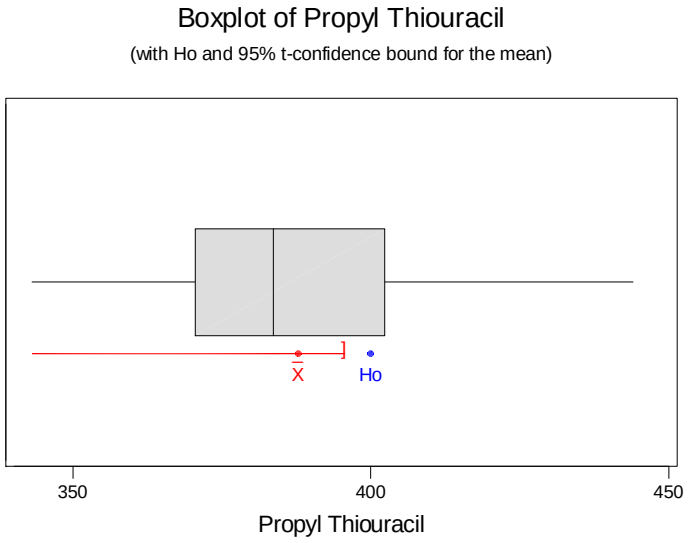
- Performs a one-sample t-test for mu less than TARGET &
  What is the target value for X 3
  DATA> 400

One-Sample T: Propylthiouracil

Test of mu = 400 vs mu < 400

Variable	N	Mean	StDev	SE Mean
Propylthiouracil	33	387.83	26.69	4.65

Variable	95.0% Upper Bound	T	P	
Propythiouracil	395.70	-2.62	0.007	**



Outliers are < Median-3*IQD OR > Median+3*IQD

Boundary for outliers are values < 288.461 and > 478.870

No outliers

- Transforms data to natural log

Week	Rep	Ln(Concentration)
0	1	5.9642
0	2	6.0036
0	3	5.9295
0	1	5.9991
0	2	6.0399
0	3	6.0671
1	1	5.9893
1	2	6.0855
1	3	5.9526
2	1	6.0865
2	2	5.9765
2	3	6.0958
3	1	6.0481
3	2	5.9956
3	3	5.9291
4	1	5.8576
4	2	5.8384
4	3	5.8898
5	1	5.9078
5	2	5.8890
5	3	5.9223
7	1	5.9820
7	2	5.9811
7	3	5.9173
8	1	5.9583
8	2	5.9246
8	3	5.9167
9	1	5.9300
9	2	5.9294
9	3	5.8900
12	1	5.9498
12	2	5.9137
12	3	5.8644

- Conducts Simple Linear Regression

Regression Analysis: Propythiouracil versus Week

The regression equation is
Propythiouracil = 6.00 - 0.00933 Week

Predictor	Coef	SE Coef	T	P	
Constant	6.00159	0.01613	372.12	0.000	
Week	-0.009333	0.002698	-3.46	0.002	**

S = 0.05847 R-Sq = 27.8% R-Sq(adj) = 25.5%

Analysis of Variance

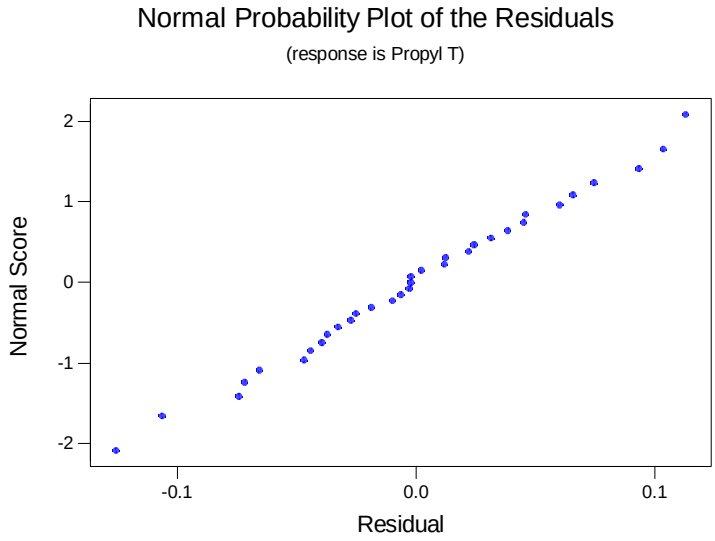
Source	DF	SS	MS	F	P	
Regression	1	0.040912	0.040912	11.97	0.002	
Residual Error	31	0.105997	0.003419			
Lack of Fit	8	0.057943	0.007243	3.47	0.009	**
Pure Error	23	0.048054	0.002089			
Total	32	0.146909				

Unusual Observations

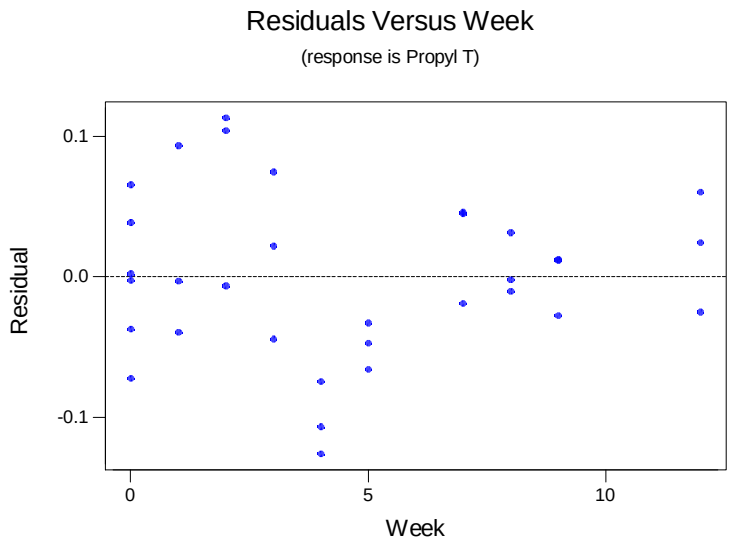
Obs	Week	Propyl T	Fit	SE Fit	Residual	St Resid
17	4.0	5.8384	5.9643	0.0103	-0.1259	-2.19R

R denotes an observation with a large standardized residual

Normplot of Residuals for Propylthiouracil



Residuals from Propyl T vs Week



Do you want to remove any data points? (yes OR no)
n

Should a quadratic be fit? (yes OR no)
n

- Power analysis for t-test of slope less than zero

Power and Sample Size

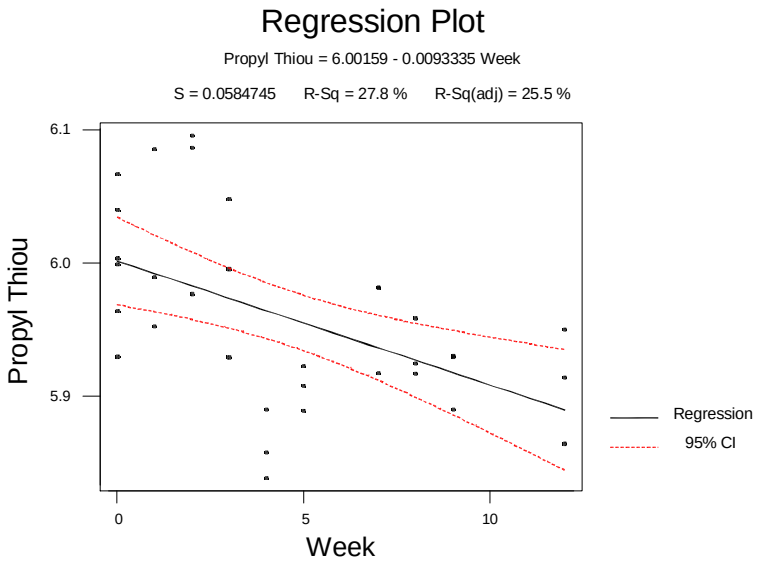
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05 Sigma = 0.0584745

Sample Size	Power	Difference
31	0.9900	-0.0427

- That means we would detect a mean of 5.949 as significantly less than ln(400) = 5.991 or a change of 383.3 from 400 = 4.2% loss.

- Fit 95% confidence bands about the fitted simple linear model



- **Conclusion – only 9 data points were greater than the target concentration of 400 mg/mL, however, the average day 0 concentration was 404, thus stability was evaluated using the target concentration. The slope through time was significant and the concentration was expected to stay above 90% of the target concentration for only 8 weeks. Thus, the chemical is stable for only 8 weeks.**

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Propylthiouracil in-life test suspension samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Propylthiouracil in corn oil

TEST SOLUTION, SAMPLE CUSTODY, AND PROCESSING:

Test suspension samples were prepared by the EDSP Chemical Repository, Sequim, WA, using Propylthiouracil (PTU) (CF 1823, TCI America lot # GB01, expiration date 10/04) suspended in Mazola corn oil (corn oil was from containers with the following expiration dates: 6/12/03, 1/1/04, and 4/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time.

Test suspensions of PTU (CAS 51-52-5) supporting EDSP WA 2-14 were made on 11/20/02 (females) and 01/22/03 (males) at two test concentrations (0.4 and 5.0 mg/mL) for female and male rat exposures. The 0.4 mg/mL concentration was prepared by weighing 0.080 g of PTU (CF 1823, TCI America, Lot # GB01, expiration date 10/04) into a 250 mL, wide-mouth, amber glass bottle after sieving through an 80-mesh screen and adding 186 g corn oil to obtain the desired concentration. The same approach was used for the second concentration: 1.0 g PTU was weighed after sieving and 185 g corn oil added to obtain the 5.0-mg/mL concentration. The samples were stirred and stored in a refrigerator prior to shipping. Samples were collected to verify test concentrations on 11/20/02, analyzed on 11/21/02 (Table 1), and also collected and analyzed on 01/23/03 (Table 2). For female exposures, Replicate 1 samples were shipped on 11/21/02 and Replicate 2 samples on 11/25/02. For male exposures, Replicate 1 samples were shipped on 01/23/03 and Replicate 2 samples on 01/27/03.

The test solution was sampled four times during the female test (11/27/02, 12/03/02, 12/10/02, and 12/17/02) and five times during the male test (1/26/03, 2/2/03, 2/9/03, 2/16/03, 2/23/03). Data are reported in Table 3 for males and Table 4 for females. Table 5 provides results of analysis of remaining formulation samples after dosing to assess changes in test solution concentrations from the beginning and end of the test.

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:

Triplicate 1 mL samples from the top (about 0.25 inches below the surface) and bottom (about 1 inch from the bottom) of the container were sampled and placed in a tared, 30 mL, amber-glass bottle. At this time, the sample weight was determined gravimetrically. Then 25 mL sodium hydroxide (NaOH) in deionized (DI) water was added. The alkaline water was prepared from 6.0 mL of a 50% by weight NaOH in water diluted to 1 L. The container was agitated for about 3 min to mix. Then, 3 mL of solution was transferred

to a syringe with a Gelman acrodisk CR, PFTE 0.2-µm filter attached. The filtered solution was placed into a 2 mL auto sampler vial, and 0.5 mL removed and placed into a 5 mL cuvette that works with the Beckman DU8 spectrophotometer. 1.5 mL of the alkaline water solution was added to the sample, the cuvette was swirled to mix, and the sample was analyzed using the Beckman DU8 spectrophotometer with an ultraviolet/visible (UV/VIS) detector at the 260 nm wavelength with a slit-width of 0.5 and the average read time set to 3. The unknown absorption is compared with that of the calibration standards. Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1197, A-E, and a continuing calibration blank and a continuing calibration verification (CCV) sample analyzed at the beginning and end of every run.

In-life and Returned Container Samples:

Samples were returned from RTI at two different times: 12/18/02 for female rat assays (received at Battelle, Sequim, WA, on 12/20/02) and 03/04/03 for male rat assays (received at Battelle, Sequim, WA, on 03/05/03). The samples were removed from the refrigerator, allowed to warm to room temperature, stirred using a stir plate and stir bar, and 1 mL sampled and placed in a tared, 25 mL, amber-glass vial. The weight of the samples was determined gravimetrically. 25 mL of a 3-g/L NaOH:water solution (6.0 mL of a 50% by weight NaOH in water diluted to 1 L) was added and the solution agitated by hand for 3 min. Samples returned from RTI in 20 mL scintillation vials were not subsampled; the entire sample was used. The scintillation vial was weighed, the solution poured into a 25 mL, amber glass vial, and 10 mL of alkaline solution added. The vial was capped, agitated, and then poured into an amber glass vial. The process was repeated using 15 mL of alkaline solution, and the scintillation vial was cleaned with one rinse of methanol (MeOH, JT Baker, lot # 47E43) and one rinse of methylene chloride (MeCl, JT Baker, lot #X36E04), and then allowed to dry. The empty vial was re-weighed to obtain the sample weight. Two corn-oil blanks were prepared using Mazola corn oil (Battelle CMS bar code 172653).

Two (2.0) mL of the solution was filtered using a syringe with a Gelman acrodisk CR, PFTE 0.2 µm filter attached. The filtered solution was placed into a 2 mL auto sampler vial, and about 0.5 mL removed and placed into a 5 mL cuvette that works with the Beckman DU8 spectrophotometer. 1.5 mL of the alkaline water solution was added to the sample, the cuvette swirled to mix, and the sample analyzed using the Beckman DU8 spectrophotometer with a UV/VIS detector at the 260 nm wavelength, with a slit-width of 0.5, and the average read time set to 3. The unknown absorption was compared with that of the calibration standards. Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1197, A-E, and a blank and a CCV sample analyzed at the beginning and end of every run.

SAMPLE ANALYSIS: The samples were analyzed by a modified SW 846 method, 9065, using a Beckman DU8 spectrophotometer with a UV/VIS detector at the 260nm wavelength, with a slit width of 0.5 and the average read time set to 3.

Data Quality Objectives	Control Limits
Procedural Blank	<5 X MDL
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: Modified SW 846 method, 9065, using a Beckman DU8 spectrophotometer with a UV/VIS detector at the 260 nm wavelength, with a slit-width of 0.5 and the average read time set to 3.

CALIBRATION: Calibration with a five-point curve was conducted using dilutions prepared from calibration standard PP-1197, A-E, and a blank and a CCV sample analyzed at the beginning and end of every run.

CONTINUING STANDARD RECOVERY: Percent recovery results for three initial and five CCV samples analyzed with the in-life sample data set ranged from 97% to 108% with a mean recovery of 97%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK: PTU was not detected above five times the detection limit in the seven blanks analyzed with the test solution and in-life samples.

DETECTION LIMIT: The PTU detection limit was 50.6 µg/mL as determined by an MDL study using the low calibration standard (0.5055 µg/mL) reported with the data. No data below this value were reported.

BLANK SPIKE SAMPLES: Blank spike samples were not analyzed.

REPLICATE ANALYSIS: The percent relative standard deviations (% RSD) for the two test solutions prepared on 11/20/02 were 4.7% for the 0.40-mg/mL replicates and 2.64% for the 5.0-mg/mL replicates.

The % RSD for the two test solutions prepared on 01/22/03 were 6.4% for the 0.40-mg/mL replicates and 4.9% for the 5.0-mg/mL replicates.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of PTU Test Solution Concentrations Prepared on 11/20/2002 and Analyzed on 11/21/02

Nominal Conc.	Sample ID Number	Dilution	Measured Conc. (mg/mL)	Blank-Corrected Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	% RSD
	1823-1b-2-6 Blank R-1	4	0.0899	NA		
	1823-1b-2-6 Blank R-2	4	0.0591	NA		
	1823-1b-2-6 Blank R-3	4	0.0441	NA		
0.4 mg/mL	WA 2-14-T-F Rep1 R-1	4	0.533	0.468		
0.4 mg/mL	WA 2-14-T-F Rep1 R-2	4	0.491	0.426	0.447	4.7%
0.4 mg/mL	WA 2-14-T-F Rep1 R-3	4	0.511	0.447		

	1823-1b-2-6 Blank R-2 100 µL	20	0.0579			
5.0 mg/mL	WA 2-14-V-F Rep1 R-1	20	4.56	4.51		
5.0 mg/mL	WA 2-14-V-F Rep1 R-2	20	4.80	4.74	4.65	2.64%
5.0 mg/mL	WA 2-14-V-F Rep1 R-3	20	4.76	4.70		

Table 2. Verification of PTU Test Solution Concentrations Sampled and Analyzed on 01/23/03

Nominal Conc.	Sample ID Number	Dilution	Measured Conc. (mg/mL)	Blank-Corrected Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	%RSD
	Corn oil blank 1g 0.5 mL/1.5mL	4	0.054	NA		
0.4 mg/mL	Sent to RTI 2-14 B-M Rep 1	4	0.518	0.464		
0.4 mg/mL	Sent to RTI 2-14 B-M Rep 2	4	0.473	0.419	0.432	6.4%
0.4 mg/mL	Sent to RTI 2-14 B-M Rep 3	4	0.467	0.413		
	Corn oil blank 1g 0.1 mL/1.9mL	4	0.029	NA		
5.0 mg/mL	Sent to RTI 2-14 C-M Rep 1	20	4.72	4.69	4.95	4.9%
5.0 mg/mL	Sent to RTI 2-14 C-M Rep 2	20	5.20	5.17		
5.0 mg/mL	Sent to RTI 2-14 C-M Rep 3	20	5.03	5.00		

Table 3. PTU In-life Sample Concentrations - Males

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Blank Corrected[(a)] Measured Conc. (mg/mL)	% of Nominal
01/26/03	03/05/03	05/23/03	0.4 mg/mL	1-26-03 PND 23 2-14-B-M	0.350	88%
02/02/03	03/05/03	05/23/03	0.4 mg/mL	2-2-03 PND 30 2-14-B-M	0.347	87%
02/09/03	03/05/03	05/23/03	0.4 mg/mL	2-9-03 PND 37 2-14-B-M	0.299	75%
02/16/03	03/05/03	05/23/03	0.4 mg/mL	2-16-03 PND 44 2-14-B-M	0.347	87%
02/23/03	03/05/03	05/23/03	0.4 mg/mL	2-23-03 PND 51 2-14-B-M	0.333	83%
01/26/03	03/05/03	05/23/03	5.0 mg/mL	1-26-03 PND 23 2-14-C-M	4.44	89%
02/02/03	03/05/03	05/23/03	5.0 mg/mL	2-2-03 PND 30 2-14-C-M	5.41	108%
02/09/03	03/05/03	05/23/03	5.0 mg/mL	2-9-03 PND 37 2-14-C-M	4.82	96%
02/16/03	03/05/03	05/23/03	5.0 mg/mL	2-16-03 PND 44 2-14-C-M	4.60	92%
02/23/03	03/05/03	05/23/03	5.0 mg/mL	2-23-03 PND 51 2-14-C-M	4.16	83%

(a) Associated blank data are reported in raw data files

Table 4. PTU In-life Sample Concentrations – Females

Date Sample Collected	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Blank Corrected[(a)] Measured Conc. (mg/mL)	% of Nominal
11/27/02	12/20/02	01/22/03	0.4 mg/mL	In-Life 11-27 2-14 T-F	0.344	86%
12/03/02	12/20/02	01/22/03	0.4 mg/mL	In-Life 12-03 2-14 T-F	0.359	90%
12/10/02	12/20/02	01/22/03	0.4 mg/mL	In-Life 12-10 2-14 T-F	0.388	97%
12/17/02	12/20/02	01/22/03	0.4 mg/mL	In-Life 12-17 2-14 T-F	0.351	88%
11/27/02	12/20/02	01/22/03	5.0 mg/mL	In-Life 11-27 2-14 V-F	4.95	99%
12/03/02	12/20/02	01/22/03	5.0 mg/mL	In-Life 12-03 2-14 V-F	4.19	84%
12/10/02	12/20/02	01/22/03	5.0 mg/mL	In-Life 12-10 2-14 V-F	4.90	98%
12/17/02	12/20/02	01/22/03	5.0 mg/mL	In-Life 12-17 2-14 V-F	3.69	74%

(a) Associated blank data are reported in raw data files

Table 5. PTU Post-Test Sample Concentrations for Formulations Returned to Battelle from RTI

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Blank-Corrected[(a)] Measured Conc. (mg/mL)	% of Nominal
11/20/02	12/20/02	01/22/03	0.4 mg/mL	From RTI, 2-14 T-F Remainder	0.393	98%
01/22/03	03/05/03	05/23/03	0.4 mg/mL	WA 2-14-B-M Rep 3 Remainder	0.494	124%
11/20/02	12/20/02	01/22/03	5.0 mg/mL	From RTI, 2-14 V-F Remainder	4.71	94%
01/22/03	03/05/03	05/23/03	5.0 mg/mL	WA 2-14-C-M Rep 3 Remainder	5.22	104%

(a) Associated blank data are reported in raw data files

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-003; Atrazine, DDE, Methoxychlor, phenobarbital, propylthiouracil, ketoconazole, Linuron, fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[ ]	Protocol
[ ]	SOP	[ ]	Method	[X]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: The protocol for WA 2-14 does not provide holding times for analysis of in-life samples. The stability of formulations was determined to be adequate for the period of time that animals would be dosed.

DEVIATION: In-life samples were not analyzed within the stability time determined during the testing of the stability of the formulation.

REASON/IMPACT: No impact. The formulations were shown to be within the acceptable target range based on established preparation procedures and were used within the known stability time periods determined for each formulation.

PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action is required beyond this documentation.

ACTIONS TO PREVENT RECURRENCE: Upper management will review testing schedules for return shipments and analysis.

Approval:

Michael Blanton,
WAL — Date 11/3/03

Eric Crecelius,
Study Director
Chemical Repository — Date 11/3/03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Chemical Repository Services for the EDSP

EPA Contract No. 68-W-01-023

Chemistry Report for WA 2-14
Vinclozolin in Mazola Corn Oil

November 11, 2003

Prepared By:

Eric A. Crecelius, Ph.D.
Chemical Repository Manager

11/11/03
Date

Approved (One-over-one) By:

Richard M. Ecker
Director, Marine Sciences Laboratory

11/11/03
Date

Battelle Marine Sciences Laboratory
1529 West Sequim Bay Road
Sequim, WA 98382

Submitted to:

Dr. Julia George

Center for Life Sciences and Toxicology
Research Triangle Institute

PO Box 12194

Research Triangle Park, NC 27709

Chemistry Report for WA 2-14
Vinclozolin in Mazola Corn Oil

Reviewed by: Deborah Coffey

Deborah Coffey, Quality Assurance Officer

Battelle Marine Sciences Laboratory

Date: 11-18-03

Chemistry Report for WA 2-14
Vinclozolin in Mazola Corn Oil

Parameter	Chemical
Compound Name	Vinclozolin
CAS #	50471-44-8
Central File No.	CF-1828
Initial Receipt Date	5/30/2002
Expiration Date	4/2005
Manufacturer	ChemService, Inc
Lot Number	281-94A
Battelle Study #	WA 2-14-02-01
Method	SW 846, 8015B Modified

Executive Summary

The chemical purity of vinclozolin determined by the manufacturer was 99%. The purity result from Battelle-Sequim by GC-FID was determined to be 99.7%. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of vinclozolin was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 22 weeks. Thus, stability testing of the vinclozolin stock solution in corn oil was considered stable at the 6 mg/mL concentration for the required testing period of 4.5 weeks. Stability information for vinclozolin at 20 mg/mL can be found in *Report on One-Generational Extension Study of Vinclozolin and Di-n-Butyl Phthalate Administered by Gavage on Gestational Day 6 to Postnatal Day 20 CD© (Sprague-Dawley) Rats* (EPA Contract Number 68-W-01-023, Work Assignment 2-10, May 7, 2002). Vincozolin in corn oil at 20 mg/mL was also considered stable for the required 4.5 week test duration.

Mazola corn oil (expiration dates 4-03 and 9-03) were purchased on 9-04-01 and 6-17-02 from local grocery stores, Mark and Pack and Quality Foods Center respectively, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 6-17-02 in triplicate as an indicator of decomposition. The average peroxide number in the Mazola corn oil with an expiration date of 4-03 was 2.07 meq/kg (RSD = 5.9%). The average peroxide number in the Mazola corn oil with an expiration date of 9-03 was 1.38 meq/kg (RSD = 7.8%). This level of peroxide is consistent with the request that the oil have a peroxide number less than 3 meq/kg.

The in-life sample vials were returned empty. The concentrations of vinclozolin in post-test formulation samples ranged from 90% to 95% of the nominal concentration.

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1.0 INTRODUCTION

The goal of the Battelle-Sequim, Marine Sciences Laboratory (MSL) Chemical Repository for the Endocrine Disruptor Screening Program (EDSP) is to provide the participating laboratory with requested chemicals of documented quality at required concentrations and in a matrix appropriate for different toxicological tests. The EDSP Chemical Repository supplies the manufacturer's information regarding purity and stability, the material safety data sheet (MSDS) chemical information, and independent analysis of purity and stability in a matrix specified by the Purity and Stability Testing Plan made in collaboration with the requesting Principal Investigator. Additional analysis associated with the in-life studies are also provided when requested. This report is the product of such a request.

Under Work Assignment (WA) 2-14 and Battelle-Sequim Study Number WA 2-14-02-01, Dr. Julia George from Center for Life Sciences and Toxicology, Research Triangle Institute, requested purity and stability testing of vinclozolin (Figure 1). Electronic files submitted to the EDSP Data Coordination Center in support of this work assignment are CRF_WA-2-14_vinclozolin-cornoil.doc, PSTP_WA-2-14_vinclozolin-cornoil.doc, DSUM_WA2-10_2-14_2-23.xls, and DAF_WA2-10_2-14_2-23.doc.

2.0 GENERAL METHODS

Methods of standard operation of the Chemical Repository are addressed in the procedure, EDSP.C-001-01, The EDSP Chemical Repository. This procedure addresses chemical procurement including procurement of controlled substances, when applicable, which have unique permitting, ordering, handling, inventory, and storage requirements; chemical receipt and chain of custody, chemical log-in and labeling, inventory, chemical storage; stock solution preparation, documentation and archiving; test solution preparation, documentation and shipping; chemical disposal, and repository maintenance over time. The quality assurance (QA) requirements for procurement of chemicals for use in the Chemical Repository are addressed in procedure, MSL-A-012, Procurement. Each purchase requisition receives QA review to determine what is being ordered and which specific requirements apply.

2.1 Chemical Procurement

As requested by Dr. Julia George, vinclozolin, (CAS No. 50471-44-8) was purchased for purity and stability analysis and a pubertal study on rats (Figure 1). Vinclozolin was purchased from ChemService, Inc and lot number 281-94A was initially received on 5/30/2002 with an expiration date of 4/2005 (Table 1). The chemical was left in the original container, logged in to the Chemical Management System (CMS) and given a CMS barcode and unique log in number (CF-1828) as per the QA Project Plan (QAPP) for the EDSP Chemical Repository. The chemical was stored in a cool, dry location at room temperature, away from direct sunlight.

Corn oil (expiration dates 4-03 and 9-03) was purchased on 9-04-01 and 6-17-02 from local grocery stores, Mark and Pack and Quality Foods Center respectively, to be used as a carrier for the stability testing. The oil had no visual defects and was stored frozen. The peroxide concentration was measured on 6-17-02 in triplicate as an indicator of decomposition following the procedures in the Battelle, Columbus SOP #CCB_IV-001-04. It was requested that the oil have a peroxide number less than 3 meq/kg. Any bottles that did not meet this requirement were discarded.

EDSP Chemical Request Form

For EPA WA: 2-14-02-01

Study Director

Name: Dr. Julia George
Affiliation: Center for Life Sciences and Toxicology
Research Triangle Institute
Location: PO Box 12194
Research Triangle Park, NC 27709
Telephone number: 919-541-5862

Bioassay Information

Proposed Bioassay: Pubertal

Test Chemical: Vinclozolin (MSL CF 1828)

Carrier(s): corn oil (Mazola)

Concentrations/Dilution Series: 6 mg/mL and 20 mg/mL

*Consider if analysis method detection limit which may be determined in
Purity analysis is above or below desired test concentrations?

In vitro or in vivo tests? In vivo

Organism to be tested: rat

Method of test solution administration: oral gavage

Planned/proposed test duration: 4.5 weeks

Chemical Information

Chemical Name: Vinclozolin

CAS: 50471-44-8

Any known purity information: may refer to attached documentation	Manufacturer's Purity Information: 99% pure
Any known stability information: may refer to attached documentation	None available
Desired purity (%) for test? 95% or greater	

Figure 1. EDSP Requisition Form for Vinclozolin

Table 1. Chemical Procurement Information

Parameter	Chemical
Compound Name	Vinclozolin
CAS #	50471-44-8
Central File No.	CF-1828
Initial Receipt Date	5/30/2002
Expiration Date	4/2005
Manufacturer	ChemService, Inc
Lot Number	281-94A
Manufacturer's Purity	99%
Storage Conditions	Cool, dry place/room temp.
Battelle Study #	WA 2-14-02-01
Method	SW 846, 8015B Modified

2.2 Chemical Purity

Chemical purity was verified by chromatographic analysis to determine areas under peaks other than the principal peak and then compared to the manufacturer's certificate of analysis/purity (Appendix A). No statistical analyses were performed for the verification of chemical purity. General methods are documented in the procedure, EDSP.D-012-01, Chemical Repository Summary Displays and Statistical Analyses for the EDSP Data Coordination Center (DCC).

Purity verification was conducted by making a solution in hexane of about 100 µg/mL. This matrix was then run on a gas chromatograph with a flame ionization detector (GC-FID). A hexane blank was also run on the GC-FID. The purity was determined by first identifying the peaks in the chromatogram of the Vinclozolin that are the same as the peaks in the analysis of the blank hexane sample. The areas associated with these common peaks were then eliminated by inhibiting integration and the remaining peaks were reported as a percentage of the total peak area. The percentage associated with the largest peak represented the purity of vinclozolin. The GC was set up with an auto sampler and a 30 m x 0.25 mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and the detector temperature at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution. One replicate was analyzed.

2.3 Preparation of Stock Matrices for Stability Analysis

A general study plan for stability testing based on the WA 2-14 request from Dr. Julia George was developed as the stability test protocol and is presented in Appendix B. A single stock solution was prepared to arrive at the chemical concentration requested for stability analysis (Table 2). Stability information for vincozolin at 20 mg/mL can be found in *Report on One-Generational Extension Study of Vinclozolin and Di-n-Butyl Phthalate Administered by Gavage on Gestational Day 6 to Postnatal Day 20 CD© (Sprague-Dawley) Rats* (EPA Contract Number 68-W-01-023, Work Assignment 2-10, May 7, 2002). All samples were analyzed in triplicate so that a mean concentration and relative standard deviation (RSD) could be determined. General methods are documented in EDSP.D-012-01.

The Vinclozolin stock matrix was prepared on 6-18-02 for testing as described in Table 2. Briefly, for the 6 mg/mL vinclozolin, 0.3018 g was weighed into a 50 mL Class A volumetric flask and corn oil was added to the 50 mL mark. The solution was agitated by hand shaking for approximately five minutes until all of the vinclozolin was dissolved. All solutions

Table 2. Stock Matrix Composition for Stability Testing

Study and Duration	Test Chemical	Target Concentration	Sample ID	Stock Matrix
WA 2-14-02-01 12 Weeks	Vinclozolin	6 mg/mL	1828-1b	0.3018 g in 50 mL Mazola corn oil

were transferred to ashed, amber glass bottles. Bottles were labeled and stored at 4ºC ± 2ºC for the duration of the test.

Density of the Mazola corn oil was measured as 0.92 g/mL for these samples. Using an Excel spreadsheet, the weight of corn oil was converted to a volume (i.e., g corn oil / density). Lower and upper 95% confidence bounds on the density of corn oil from a sample of two lots were estimated as 0.89 and 0.93 g/mL respectively.

2.4 Analytical Chemistry for Stability Testing

Chemical stability was evaluated under storage conditions and matrix specifications as requested by the participating laboratory. At initiation and at each time period throughout the duration of the test, the concentration was determined by chromatographic analysis. Triplicate aliquots of the stock solution were tested. The frequency of determinations and the duration of testing were determined by the requesting principal investigator and the chemists based on *a priori* knowledge about chemical stability. General methods are documented in EDSP.D-012-01.

Vinclozolin stock solution was sampled by weighing ~1 g of sample into a 30 mL amber, ashed vial and adding 25 mL of hexane using a volumetric pipette. For sample 1828-1b, analysis was then conducted by taking 0.1 mL of the hexane solution and 0.02 mL of internal standard REP7, 5a androstane and 0.88 mL of hexane to the GC auto sampler vial. A corn oil blank was prepared in the same way. This solution was then run on the GC-FID for quantification. The major peak determined during the purity analysis of vinclozolin was used for this analysis. Continuing calibration verification (CCV) samples were analyzed to demonstrate on-going calibration accuracy.

2.5 Statistical Analysis of Stability

Log linear degradation curves were fitted to the data to describe the chemical concentration vs. time trends and their dependence on storage conditions and solvent matrix. Lack of fit and residual plots were evaluated to determine the form of the regression. Power calculations based on the observed variability were used to determine the sensitivity of the test to detect degraded concentrations. General methods are documented in SOP EDSP.D-012-01.

2.6 Analytical Chemistry for In-Life Testing

Analytical methods associated with in-life testing were similar to those described in Section 2.4.

3.0 RESULTS

3.1 Chemical Purity

Battelle-Sequim ran a GC-FID purity scan on the vinclozolin. The chromatogram, after solvent blank correction, showed one large peak that had the appropriate retention time for vinclozolin and several very small peaks. The area of the vinclozolin peak was 99.7% of the total area of all peaks in the chromatogram. Chemical purity of vinclozolin determined by the manufacturer was 99% (Appendix A).

3.2 Analytical Chemistry for Stability Testing

Chemical stability testing was initiated on 6-18-02. Chemical concentration was determined 11 times over a period of 12 weeks. The analytical and quality control (QC) results are presented in Appendix C. A single preparation blank was analyzed with every batch for QC purposes. There were no detectable concentrations of vinclozolin in the blanks. CCV results ranged from 99.4% to 101%. Internal standards were analyzed with each sample and these results ranged from 101% to 111%. The MDL was 115 µg/mL.

Both lots of Mazola corn oil had peroxide numbers less than 3 meq/kg as required for biological testing (Appendix C). The average peroxide number in the Mazola corn oil with an expiration date of 4-03 was 2.07 meq/kg (RSD = 5.9%). The average peroxide number in the Mazola corn oil with an expiration date of 9-03 was 1.38 meq/kg (RSD = 7.8%).

3.3 Statistical Results of Stability Trial

A plot of vinclozolin with a target concentration of 6,000 µg/mL against time suggests very little chemical decay (Figure 2). There were no data points below 90% of the target concentration. Based on the final regression model and the lower 95% confidence limit of the slope, the concentration of vinclozolin was expected to stay greater than or equal to 90% of the target concentration for up to an estimated 22 weeks (Table 3). Thus, this stock solution was considered stable for the required 4.5-week testing period. The complete statistical analysis is presented in Appendix D.

3.4 Chemistry Results for the Analysis of In-Life Samples

The in-life sample vials were returned empty. The concentrations of vinclozolin in post-test formulation samples ranged from 90% to 95% of the nominal concentration. The complete analysis is presented in Appendix E.

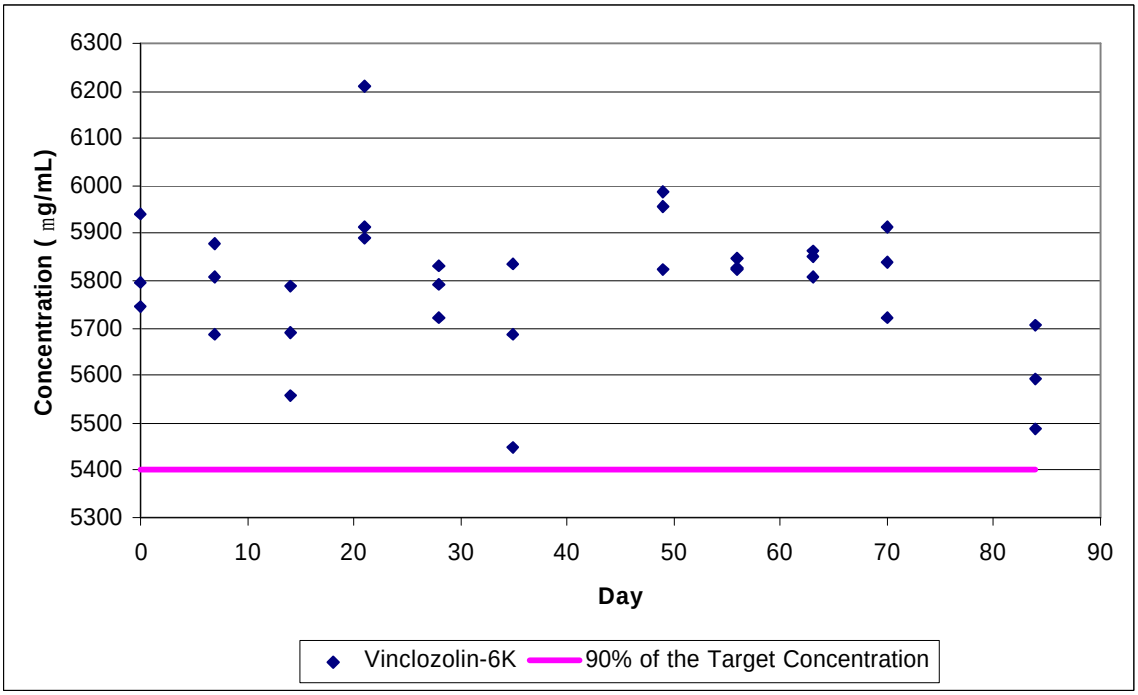


Figure 2. Observed Concentration of Vinclozolin with a Target Concentration of 6,000 mg/mL Against Time

Table 3. Summary of Statistical Results for Vinclozolin

WA 2-14-02-01 **Statistical Analysis conducted by Valerie Cullinan** **Using Minitab Version 13.32, Minitab Inc., 1999.**	**1828-1b** **Vinclozolin-6K**
Target Concentration (μg/mL)	6000
Number of determinations	1
Number of days tested	84
Number of replicates per day	3
Number of outliers removed	0
Number of observations removed	0
Overall Mean Concentration	5796
95% Upper CL	5839
error degrees of freedom	32
1-sample t-test of Ho: μ >= Target	S[a]
estimated intercept of ln(concentration) against time	8.6702
estimated slope of ln(concentration) against time	-0.0001
standard error of slope	0.0002
error degrees of freedom	31
Significance test of lack-of-fit for final model	S
Significance test of Ho: β = 0 vs. H1: β = 0	NS[b]
Lower 95% CL of β	-0.0005
Upper 95% CL of β	0.0002
Maximum Percent Loss (using LCL)	0.4%
Mean Percent Loss (using bhat)	0.1%
LN(90% of Target)	8.5942
Number of days until at 90% of Target (using LCL)	156
Conclusion using Target Concentration:	**Stable for 4.5 wks**

[a] Significant at α = 0.05
[b] Not significant at α = 0.05

4.0 CONCLUSIONS

Stability testing of vinclozolin in corn oil concluded that the chemical was stable at 6 mg/mL for a period of 4.5 weeks. Chemical purity of vinclozolin determined by the manufacturer was 99%; purity determined by Battelle-Sequim was 99.7%. Stability information for vinclozolin at 20 mg/mL can be found in *Report on One-Generational Extension Study of Vinclozolin and Di-n-Butyl Phthalate Administered by Gavage on Gestational Day 6 to Postnatal Day 20 CD© (Sprague-Dawley) Rats* (EPA Contract Number 68-W-01-023, Work Assignment 2-10, May 7, 2002). Vinclozolin in corn oil at 20 mg/mL was also considered stable for the required 4.5 week test duration.

The level of peroxide measured in corn oil used for the stability trial was consistent with the request that the oil have a peroxide number less than 3 meq/kg.

The in-life sample vials were returned empty. The concentrations of vinclozolin in post-test formulation samples ranged from 90% to 95% of the nominal concentration.

APPENDIX A

MANUFACTURER'S CERTIFICATE OF ANALYSIS/PURITY

660 Tower Lane • P.O. Box 599 • West Chester, PA 19381-0599
1-800-452-9994 • 1-610-692-3026 • Fax 1-610-692-8729
info@chemservice.com • www.chemservice.com

CERTIFICATE OF ANALYSIS

INVOICE #: CS228928
PO #: 11113499EAC

CATALOG #: PS-1049 CAS #: 50471-44-8

DESCRIPTION: Vinclozolin

LOT #: 281-94A

PURITY: 99%

EXPIRATION DATE: 04/05

Chem Service, Inc. guarantees the purity of this chemical ± 0.5% deviation prior to the expiration date shown on the label and exclusive of any customer contamination.

Two or more of the following methods of analysis are used to determine purity: Melting point, refractive index, titration, IR, TLC, GC/FID, GC/TCD, GC/ECD, GC/MS, HPLC or DSC.

Our standards are suitable for use with all EPA methods.

Certified By:

John Conrad

John Conrad
CSM/TC

660 Tower Lane • P.O. Box 599 • West Chester, PA 19381-0599
1-800-452-9994 • 1-610-692-3026 • Fax 1-610-692-6729
info@chemservice.com • www.chemservice.com

CERTIFICATE OF ANALYSIS

CAS #: 50471-44-8

CATALOG #: PS-1049

DESCRIPTION: Vinclozolin

LOT #: 270-71B

PURITY: 98%

EXPIRATION DATE: 08/04

Chem Service, Inc. guarantees the purity of this chemical ± 0.5% deviation prior to the expiration date shown on the label and exclusive of any customer contamination.

Two or more of the following methods of analysis are used to determine purity: Melting point, refractive index, titration, IR, TLC, GC/FID, GC/TCD, GC/ECD, GC/MS, HPLC or DSC.

Our standards are suitable for use with all EPA methods.

Certified By:

John Conrad

John Conrad
CSM/TC

ISO 9001

APPENDIX B

PURITY AND STABILITY TESTING PLAN

EDSP Purity Analysis and Stability Testing Plan for Vinclozolin

Chemical Name: Vinclozolin (MSL CF Login 1828)

CAS Number: 50471-44-8

Lot Number: Lot 281-94A - two bottles, 10g and 3g, stored at RT in Bldg5 Rm 219

Expiration date: 4/05

Manufacturer's Purity Information: 99%

Manufacturer's Stability Information: none

MSL Purity Results:
Purity (%) To be determined at MSL by GC-FID

MDL has not been determined.

Bioassay Information:

Study Director
Name: Dr. Julia George
Affiliation: RTI
Location: RTP, NC
Telephone number: 919-541-5862

Proposed Bioassay: WA 2-14

Test Chemical: Vinclozolin

CAS: 50471-44-8

Carrier(s): Corn oil

Concentrations/Dilution Series: 6 mg/mL and 20 mg/mL

Below MDL determined in Purity Analysis?

In vitro or in vivo tests? In vivo

Organism to be tested: Rat

Method of test solution administration: Oral gavage

Planned/Proposed test duration: 4.5 weeks

Design of Stability Test: 6 mg/mL in glass at 4 deg. C in the dark for 12 weeks, analyzed weekly in triplicate

Number of replicates: 3

Duration: 12 weeks, sampling each week

Other factors:
Temperature regime(s): 4 deg. C
Test container type: Glass
Light or dark: Dark except when container is removed for sampling or handling
Other

Statistical testing: Regression analysis of the slope for concentration versus time

Resulting records package:
Manufacturer's certificate of analysis or purity
MSDS
Records:

- date sample received;
- date(s) sample analyzed;
- sample matrix;
- electronic file identification codes (when applicable to identify instrument data files);
- data summary reports;
  - Chemical repository confirmatory test results of chemical identity and purity;
  - Chemical repository test results of lot-to-lot variation in chemical purity;
  - Chemical repository periodic assessment results of changes in purity of stock solutions and dilutions and generation of degradation products
- QC data reports;
- data qualifying flags; and
- dilution factor(s).

APPENDIX C

ANALYTICAL RESULTS OF STABILITY TESTING

Table C.1. Vinclozolin concentration in Mazola Corn Oil (µg/mL)

Target Conc.	Sample ID	Date	Vinclozolin	Average	RSD	Recovery[1]
6000 ug/ml	1828-1b-1-1 R-1	6/18/2002	5796			
6000 ug/ml	1828-1b-1-1 R-2	6/18/2002	5745	5827	1.73%	97.1%
6000 ug/ml	1828-1b-1-1 R-3	6/18/2002	5939			
blank	Corn Oil (T=0)	6/19/2002	115 U			
6000 ug/ml	1828-1b-1-2 R-1	6/25/2002	5806			
6000 ug/ml	1828-1b-1-2 R-2	6/25/2002	5687	5791	1.68%	96.5%
6000 ug/ml	1828-1b-1-2 R-3	6/25/2002	5879			
blank	Corn Oil (week 1)	6/25/2002	115 U			
6000 ug/ml	1828-1b-1-3 R-1	7/2/2002	5689			
6000 ug/ml	1828-1b-1-3 R-2	7/2/2002	5789	5679	2.05%	94.6%
6000 ug/ml	1828-1b-1-3 R-3	7/2/2002	5558			
blank	Corn Oil (week 2)	7/2/2002	115 U			
6000 ug/ml	1828-1b-1-4 R-1	7/9/2002	5892			
6000 ug/ml	1828-1b-1-4 R-2	7/9/2002	5913	6004	2.95%	100%
6000 ug/ml	1828-1b-1-4 R-3	7/9/2002	6208			
blank	Corn Oil (week 3)	7/9/2002	115 U			
6000 ug/ml	1828-1b-1-5 R-1	7/16/2002	5722			
6000 ug/ml	1828-1b-1-5 R-2	7/16/2002	5791	5782	0.96%	96.4%
6000 ug/ml	1828-1b-1-5 R-3	7/16/2002	5833			
blank	Corn Oil (week 4)	7/16/2002	115 U			
6000 ug/ml	1828-1b-1-6 R-1	7/23/2002	5685			
6000 ug/ml	1828-1b-1-6 R-2	7/23/2002	5449	5656	3.44%	94.3%
6000 ug/ml	1828-1b-1-6 R-3	7/23/2002	5835			
blank	Corn Oil (week 5)	7/23/2002	115 U			
6000 ug/ml	1828-1b-1-7 R-1	8/6/2002	5825			
6000 ug/ml	1828-1b-1-7 R-2	8/6/2002	5986	5923	1.45%	98.7%
6000 ug/ml	1828-1b-1-7 R-3	8/6/2002	5958			
blank	Corn Oil (week 7)	8/6/2002	115 U			
6000 ug/ml	1828-1b-1-8 R-1	8/13/2002	5824			
6000 ug/ml	1828-1b-1-8 R-2	8/13/2002	5848	5833	0.24%	97.2%
6000 ug/ml	1828-1b-1-8 R-3	8/13/2002	5826			
blank	Corn Oil (week 8)	8/13/2002	115 U			
6000 ug/ml	1828-1b-1-9 R-1	8/20/2002	5807			
6000 ug/ml	1828-1b-1-9 R-2	8/20/2002	5861	5839	0.49%	97.3%
6000 ug/ml	1828-1b-1-9 R-3	8/20/2002	5850			
blank	Corn Oil (week 9)	8/20/2002	115 U			
6000 ug/ml	1828-1b-1-10 R-1	8/27/2002	5721			
6000 ug/ml	1828-1b-1-10 R-2	8/27/2002	5837	5825	1.67%	97.1%
6000 ug/ml	1828-1b-1-10 R-3	8/27/2002	5915			
blank	Corn Oil (week 10)	8/27/2002	115 U			
6000 ug/ml	1828-1b-1-12 R-1	9/10/2002	5708			
6000 ug/ml	1828-1b-1-12 R-2	9/10/2002	5488	5596	1.96%	93.3%
6000 ug/ml	1828-1b-1-12 R-3	9/10/2002	5592			
blank	Corn Oil (week 12)	9/10/2002	115 U			

[1] Recovery is relative to the target concentration
U = Not detected at a value greater than the MDL

Table C.2. CCV Data for Vinclozolin Concentration in Mazola Corn Oil

Time	Sample Name	Vinclozolin (µg/mL)	Recovery	PD
T=0	EDSP Mix1 5 ug/ml	4.97	99.4%	0.60%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
Week 1	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
Week 2	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
Week 3	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
Week 4	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
Week 5	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.05	101%	1.00%
	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
Week 7	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
Week 8	EDSP Mix1 5 ug/ml	5.06	101%	1.20%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
Week 9	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
	EDSP Mix1 5 ug/ml	5.00	100%	0.00%
	EDSP Mix1 5 ug/ml	5.03	101%	0.60%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
Week 10	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.06	101%	1.20%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
	EDSP Mix1 5 ug/ml	5.01	100%	0.20%
Week 12	EDSP Mix1 5 ug/ml	5.04	101%	0.80%
	EDSP Mix1 5 ug/ml	5.02	100%	0.40%
	EDSP Mix1 5 ug/ml	4.98	99.6%	0.40%
	EDSP Mix1 5 ug/ml	4.99	99.8%	0.20%

Text Box C1. Calibration Standard Preparation

Calibration Standard EDSP Mix 1
Calibrations were performed using a five-point calibration curve labeled EDSP Mix 1 A thru E. This mix is used for Atrazine, Fenarimol, p,p'-DDE, Methoxychlor and Vinclozolin analyzed by GC-FID. These standards were made by serial dilutions of standards for each compound. • Atrazine standard was made by weighing 0.0499 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with Methylene chloride and labeled 1826-1-1. • Fenarimol standard was made by weighing 0.0506 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1829B-1. • p,p'-DDE standard was made by weighing 0.0501 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1832-1a-1. • Methoxychlor standard was made by weighing 0.0513 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1808-1-3. • Vinclozolin standard was made by weighing 0.0512 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane and labeled 1779-78. This analysis used an internal standard, in this case 5a androstane, which is made by weighing 0.0511 g of the neat material into a 50 mL volumetric flask. This was then diluted to the 50 mL mark with hexane, this is then labeled REP7. The EDSP Mix 1 series (A through E) was made as follows. • Solution A, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 0.02 ml REP7 added to a 10 ml volumetric flask and diluted to the mark with hexane. • Solution B, 1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution C, 0.25 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 1 ml REP7 added to a 50 ml volumetric flask and diluted to the mark with hexane. • Solution D, 0.1 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane. • Solution E, 0.05 ml of 1826-1-1, 1829B-1, 1832-1a-1, 1808-1-3, 1779-78 and 2 ml REP7 added to a 100 ml volumetric flask and diluted to the mark with hexane.

Table C.3. Internal Standards Data for Vinclozolin in Mazola Corn Oil

Sample Name	Date	5A Androstane Recovery
1828-1b-1-1 R-1	6/18/2002	107%
1828-1b-1-1 R-2	6/18/2002	105%
1828-1b-1-1 R-3	6/18/2002	104%
1828-1b-1-2 R-1	6/25/2002	102%
1828-1b-1-2 R-2	6/25/2002	103%
1828-1b-1-2 R-3	6/25/2002	103%
1828-1b-1-3 R-1	7/2/2002	104%
1828-1b-1-3 R-2	7/2/2002	105%
1828-1b-1-3 R-3	7/2/2002	108%
1828-1b-1-4 R-1	7/9/2002	102%
1828-1b-1-4 R-2	7/9/2002	102%
1828-1b-1-4 R-3	7/9/2002	104%
1828-1b-1-5 R-1	7/16/2002	106%
1828-1b-1-5 R-2	7/16/2002	107%
1828-1b-1-5 R-3	7/16/2002	104%
1828-1b-1-6 R-1	7/23/2002	107%
1828-1b-1-6 R-2	7/23/2002	111%
1828-1b-1-6 R-3	7/23/2002	106%
1828-1b-1-7 R-1	8/6/2002	103%
1828-1b-1-7 R-2	8/6/2002	102%
1828-1b-1-7 R-3	8/6/2002	102%
1828-1b-1-8 R-1	8/13/2002	105%
1828-1b-1-8 R-2	8/13/2002	105%
1828-1b-1-8 R-3	8/13/2002	106%
1828-1b-1-9 R-1	8/20/2002	104%
1828-1b-1-9 R-2	8/20/2002	105%
1828-1b-1-9 R-3	8/20/2002	105%
1828-1b-1-10 R-1	8/27/2002	107%
1828-1b-1-10 R-2	8/27/2002	108%
1828-1b-1-10 R-3	8/27/2002	108%
1828-1b-1-12 R-1	9/10/2002	101%
1828-1b-1-12 R-2	9/10/2002	105%
1828-1b-1-12 R-3	9/10/2002	105%

Table C.4. Peroxide Concentration in Mazola Corn Oil (meq/kg) measured on 6/17/02

Sample	Volume of Sodium Thiosulfate (mL)	Normality	Weight of Oil (g)	Peroxide Number	Average Peroxide Number	RSD
Blank	0.75	0.005	5.00	0.75		
Mazola Corn Oil Expiration 9-03 R-1	1.6	0.005	5.43	1.47		
Mazola Corn Oil Expiration 9-03 R-2	1.5	0.005	5.32	1.41	1.38	7.8%
Mazola Corn Oil Expiration 9-03 R-3	1.2	0.005	4.75	1.26		
Mazola Corn Oil Expiration 4-03 R-1	2.0	0.005	5.18	1.93		
Mazola Corn Oil Expiration 4-03 R-2	2.2	0.005	5.09	2.16	2.07	5.9%
Mazola Corn Oil Expiration 4-03 R-3	2.5	0.005	5.21	2.11		

APPENDIX D

STATISTICAL REPORT

WA-2-14-02-01
Statistical Analysis conducted by Valerie Cullinan
Using Minitab Version 13.32, Minitab Inc., 1999.

11/25/2002 11:22:30 AM

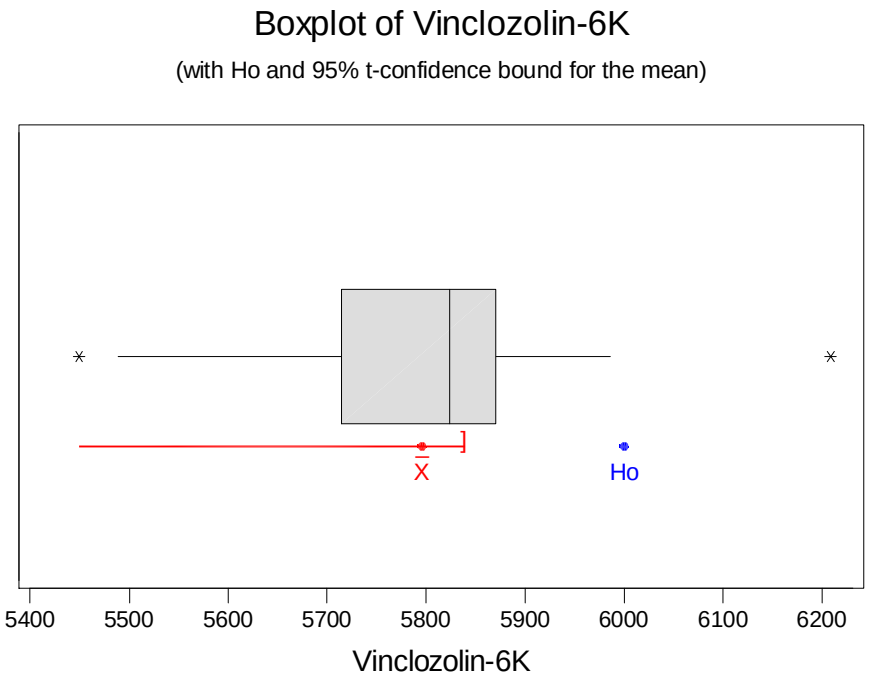
Analysis of Vinclozolin-6k in corn oil

- Test to determine if the data are from a population with mean of 6000.

One-Sample T: Vinclozolin-6K

```
Test of mu = 6000 vs mu < 6000

Variable          N      Mean     StDev   SE Mean
Vinclozolin-     33    5795.9     146.2      25.5

Variable      95.0% Upper Bound        T      P
Vinclozolin-             5839.0    -8.02  0.000
```

t Boxplot of Vinclozolin-6K



- Nonparametric Test for outlier.

```
Outliers are < Median-3*IQD OR > Median+3*IQD
Boundary for outliers are values <    5356.81  and >    6290.83
No outliers
```

- Transform data to natural logarithm and conduct regression analysis.

Week	Rep	Ln(Concentration)
0	1	8.6649
0	2	8.6561
0	3	8.6893
7	1	8.6667
7	2	8.6459
7	3	8.6792
14	1	8.6463
14	2	8.6638
14	3	8.6229
21	1	8.6813
21	2	8.6849
21	3	8.7336
28	1	8.6521
28	2	8.6641
28	3	8.6712
35	1	8.6456
35	2	8.6032
35	3	8.6716
49	1	8.6699
49	2	8.6972
49	3	8.6925
56	1	8.6697
56	2	8.6739
56	3	8.6700
63	1	8.6668
63	2	8.6761
63	3	8.6742
70	1	8.6519
70	2	8.6720
70	3	8.6852
84	1	8.6497
84	2	8.6104
84	3	8.6291

  - Conducts Simple Linear Regression

Regression Analysis: Vinclozolin-6K versus Day

The regression equation is
Vinclozolin-6K = 8.67 -0.000144 Day

Predictor	Coef	SE Coef	T	P
Constant	8.67019	0.00789	1098.93	0.000
Day	-0.0001444	0.0001684	-0.86	0.398

S = 0.02539 R-Sq = 2.3% R-Sq(adj) = 0.0%

Analysis of Variance

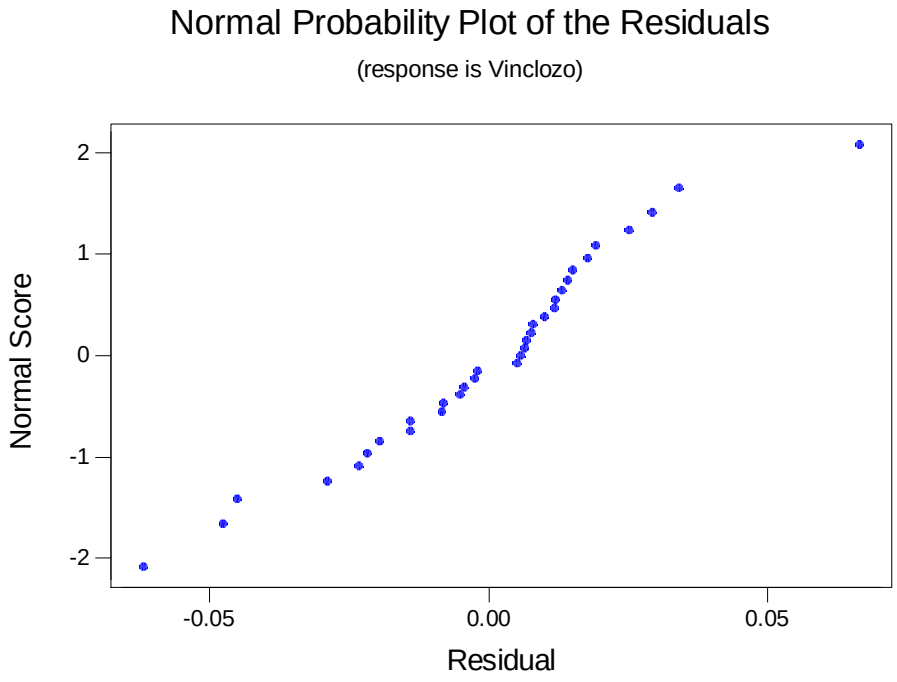
Source	DF	SS	MS	F	P
Regression	1	0.0004741	0.0004741	0.74	0.398
Residual Error	31	0.0199853	0.0006447		
Lack of Fit	9	0.0118899	0.0013211	3.59	0.007
Pure Error	22	0.0080953	0.0003680		
Total	32	0.0204594			

Unusual Observations

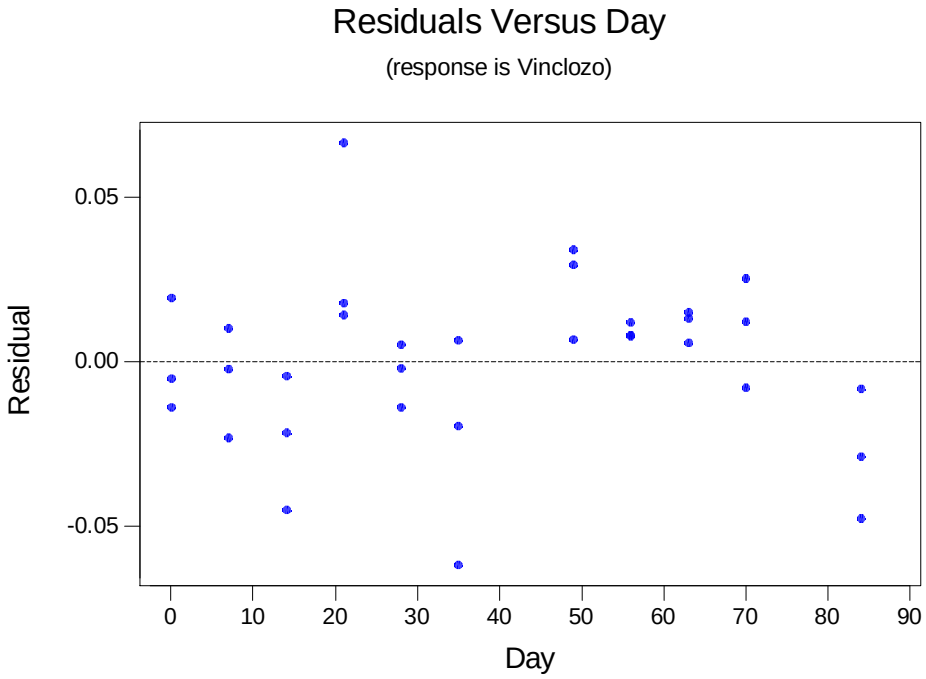
Obs	Day	Vinclozolin	Fit	SE Fit	Residual	St Resid
12	21.0	8.73363	8.66716	0.00534	0.06647	2.68R
17	35.0	8.60318	8.66514	0.00447	-0.06196	-2.48R
32	84.0	8.61040	8.65807	0.00880	-0.04767	-2.00R

R denotes an observation with a large standardized residual

Normplot of Residuals for Vinclozolin



Residuals from Vinclozolin vs Day



- Power analysis for t-test of slope less than zero

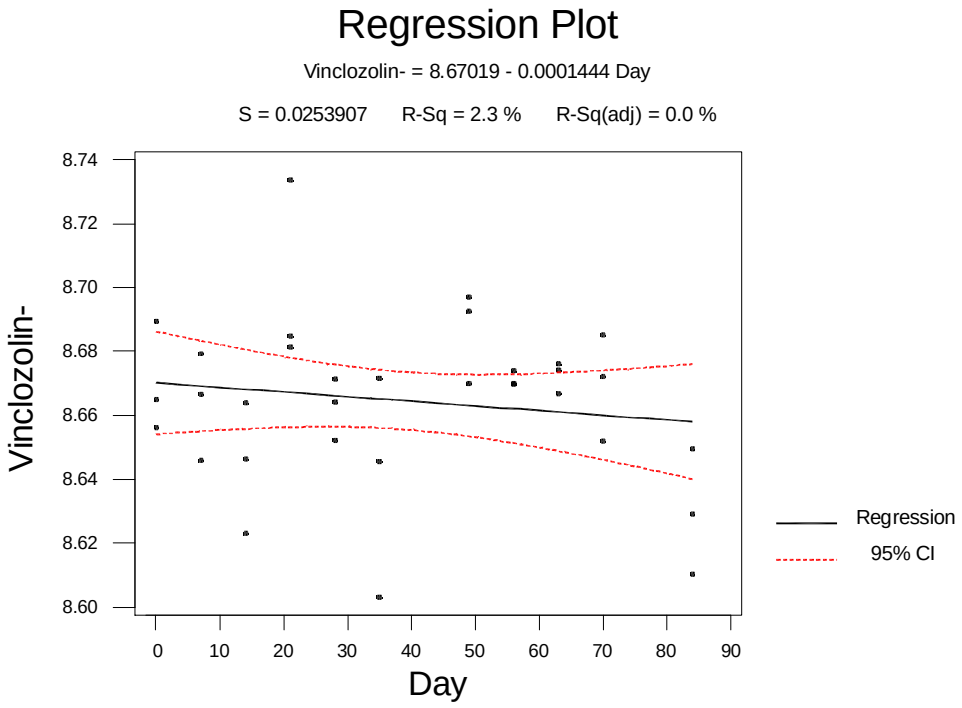
Power and Sample Size

```
1-Sample t Test

Testing mean = null (versus < null)
Calculating power for mean = null + difference
Alpha = 0.05  Sigma = 0.0253907

Sample
  Size   Power  Difference
    31  0.9900     -0.0185
```

- That means we would detect a mean of 8.6810 as significantly less than ln(6000) = 8.6995 or a change of 5890 from 6000 = 1.8% loss.

- Fit 95% confidence bands about the fitted simple linear model

Fitted Line Plot: Vinclozolin- versus Day



Conclusion – stable for 4.5 weeks.

APPENDIX E

CHEMISTRY RESULTS
FOR THE ANALYSIS OF IN-LIFE SAMPLES

Chemistry Results for Analysis of In-Life Samples

PROJECT: **EDSP WA 2-14**

PARAMETER: Vinclozolin in-life test solution samples in corn oil

LABORATORY: Battelle Marine Sciences Laboratory
1529 West Sequim Bay Rd.
Sequim, WA 98382

MATRIX: Vinclozolin in corn oil

TEST SOLUTION SAMPLE CUSTODY AND PROCESSING:

Test solution samples were prepared by the EDSP Chemical Repository, Sequim, WA, using vinclozolin (CAS 50471-44-8, CF 1828, ChemService lot # 281-94A, expiration date 4/05, 99% purity and CF 1779, ChemService lot # 270-71B, expiration date 8/04, 98% purity) dissolved in Mazola corn oil (corn oil was from containers with the following expiration dates: 6/12/03, 1/1/04, and 4/24/04). A large volume of corn oil was used because many formulations for WA 2-14 were prepared at one time. Samples were prepared at two test concentrations, 6 mg/mL and 20 mg/mL, for all replicates in the male-only exposure. The 6 mg/mL concentration was prepared by dissolving 1.2 g of vinclozolin in 185 g of corn oil in a pre-cleaned, amber glass container. The 20 mg/mL concentration was prepared by dissolving 4.0 g of vinclozolin in 182 g of corn oil.

Samples for male rat exposures were prepared at three different times:
Replicate 1 – prepared on 09/9/02 and shipped on 09/26/02
Replicate 2- prepared on 10/2/02 and shipped on 10/3/02
Replicate 3- prepared 11/03/02, shipped 11/04/02.

Note: Only samples on 09/09/02 were analyzed to verify concentration of vinclozolin. These values are reported in Table 1.

The test solution was sampled four times during the male test (10/07/02, 10/14/02, 10/21/02, and 10/28/02). The in-life sample vials were empty when received, so no data are presented. Table 2 provides results of analysis of remaining formulation samples after dosing to assess changes in test solution concentration from the beginning and end of the test.

Processing

Test Solution Samples for Concentration Verification Prior to Shipping:

The container was placed on a magnetic stir plate and stirred. 1 mL triplicate samples were removed and each placed in a tared, 60 mL, amber glass bottle. The weight of the sample was determined gravimetrically. A 1 g subsample was removed, placed in a 30 mL amber ashed vial, and 25 mL of hexane (JT Baker lot number X40E12) was added and the bottle agitated to mix. Then, 0.1 mL sample and 0.02 mL internal standard, 5a androstane, and 0.88 mL hexane were transferred to an auto sampler vial.

In-life and Returned Container Samples:

In-life and returned containers were analyzed the same way. Some of the returned containers were returned empty, so only containers with sufficient material were analyzed.

The samples were removed from the refrigerator and allowed to warm to room temperature. About 1 mL was sampled and placed in a tared, 30 mL, amber glass bottle. The weight of the sample was determined gravimetrically. 25 mL of hexane was added and the bottle agitated to mix. Then 0.1 mL was transferred to a 1.8 mL vial with 0.02 mL of internal standard solution containing 5a androstane and 0.88 mL hexane.

SAMPLE ANALYSIS

The samples were analyzed by gas chromatograph (GC) with a flame ionization detector (FID). The GC was set up with an auto sampler and a 30-m x 0.25-mm, DB-5 capillary column. The temperature program was set to start at 50ºC, and ramped at 20ºC/min to a final temperature of 320ºC. The injection port temperature was set at 270ºC and the detector temperature at 320ºC. The auto sampler was set to inject 1 µL of the matrix dilution.

Data Quality Objectives:	**Control Limits**
Procedural Blank	<5 X MDL
Blank Spike Recovery	40% - 120%
Continuing Standard Recovery	75% - 125%

QA/QC SUMMARY

METHODS: GC-FID

CALIBRATION: Calibration using a five-point curve was done using standards EDSP Mix 1 (see Appendix C) with a continuing calibration verification (CCV) sample analyzed every 10 samples.

CONTINUING STANDARD RECOVERY: Percent recovery results for initial and CCV samples analyzed with the in-life sample data set ranged from 91% to 117% with a mean recovery of 100%. There were no occurrences of recoveries exceeding the 75% to 125% acceptability range.

BLANK Vinclozolin was not detected above the detection limit in the corn oil blank analyzed with the test solution and in-life samples.

DETECTION LIMIT: The vinclozolin method detection limit (MDL) in corn oil was 115 µg/mL as determined by an MDL study. No data below this value were reported.

BLANK SPIKE SAMPLES Blank spike samples were not analyzed. In this analysis, sampling was performed by taking the sample material from flask through to analysis. Analyzing a spiked sample would be no different from analyzing a CCV.

INTERNAL STANDARD

5a androstane was spiked into each sample and analyzed as the internal standard. Average percent recovery results ranged from 99% to 103%. There were no cases in which the percent recovery of the internal standard exceeded the acceptance range of 40% to 120%.

REPLICATE ANALYSIS:

The percent relative standard deviations (% RSD) for the two test solutions ranged from 0.904 to 1.23.

Replicate samples were not submitted for the in-life sample set.

Table 1. Verification of Vinclozolin Test Solution Concentrations for Male Exposures Prepared on 09/09/02 and Analyzed on 09/12/02

Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	Replicate Mean (mg/mL)	% RSD
R-1; 09/09/02				
6 mg/mL	2-14 –J-M R-1, R-1	5.64		
6 mg/mL	2-14 –J-M R-1, R-2	5.54	5.60	0.904
6 mg/mL	2-14 –J-M R-1, R-3	5.62		
20 mg/mL	2-14 –K-M R-1, R-1	18.4		
20 mg/mL	2-14 –K-M R-1, R-2	18.9	18.7	1.23
20 mg/mL	2-14 –K-M R-1, R-3	18.8		

Table 2. Vinclozolin Post-Test Sample Concentrations for Formulations Returned to Battelle from RTI

Date Sample Prepared	Date Sample Received	Date Sample Analyzed	Nominal Conc.	Sample ID Number	Measured Conc. (mg/mL)	% of Nominal
Male Exposures						
11/03/02	11/13/02	11/22/02	6 mg/mL	WA 2-14-J-M Rep3Jar	5.72	95%
11/03/02	11/13/02	11/22/02	20 mg/mL	WA 2-14-K-M Rep3Jar	18.0	90%

Deviation Documentation Form

Project No. EDSP WA 2-14/ vinclozolin
Deviation No. WA 2-14-D-001
Project Manager: Eric Crecelius

EDSP WA 2-14 and The EDSP Chemical Repository

Entered by: Lohna O'Rourke Date: 2/12/03

The following information is (check one)
[x] a miscellaneous documentation
[ ] a deviation from Protocol, Work Plan or QA Plan (give title)

-

[ ] a deviation from SOP
(give number and title)

Description:	According to LRB 009 two lots of vinclozolin were used in the preparation of the formulations. Both lots were analyzed by Battelle for purity and were determined to be 98% or greater. However, the chemical inventory records book is not in agreement with the quantity of chemical remaining for each lot.
Corrective Action:	No corrective action.
Action to Prevent Recurrence:	Staffs that work in the Chemical Repository have received additional training on maintaining the chemical inventory records.
Impact on Project:	No impact to the project. Both lots were analyzed and had purities of 98% or greater.

APPROVED BY: Eric Crecelius 2/12/03

Eric Crecelius, Study Manager
Chemical Repository

Date

File in project notebook or study archive
Send a copy to the MSL QA Officer

ENDOCRINE DISRUPTOR SCREENING PROGRAM DEVIATION FORM

STUDY NUMBER: WA 2-14			DATE: 10/30/03		
DEVIATION NUMBER: WA 2-14-D-004: Atrazine, DDE, vinclozolin, Methoxychlor, Fenarimol			WAL/STUDY DIRECTOR: Michael Blanton/ Eric Crecelius		
NOTEBOOK NUMBER: NA					
TITLE OF STUDY: WA 2-14					
QAPP/PROTOCOL ID:					
DEVIATION RELATING TO:					
[ ]	QAPP	[ ]	QMP	[X]	Protocol
[ ]	SOP	[ ]	Method	[ ]	Miscellaneous Documentation

ORIGINAL DOCUMENT SPECIFICATIONS: 2.3 of protocol WA 2-14 states "an aliquot of each level per formulation will be analyzed"

DEVIATION: Each dose level was tested in the first preparation for each chemical. However, subsequent batches were not always analyzed.

REASON/IMPACT: No impact. Subsequent batches were prepared using the same methods and procedures as the first batches.
PROPOSED CORRECTIVE ACTION AND SCHEDULE FOR COMPLETION: No corrective action required.

ACTIONS TO PREVENT RECURRENCE: Upper management will review the analyses schedule prior to the start of the studies.

Approval:

Michael Blanton,
WAL — Date 11-3-03

Eric Crecelius,
Study Director
Chemical Repository — Date 11-3-03

Deborah Coffey,
MSL QA Manager — Date 11/3/03

Richard Ecker,
MSL Laboratory Director — Date 11/3/03

David Houchens,
EDSP Program Management — Date 10/31/03

Terri Pollock,
EDSP Battelle QAM — Date 10-31-03

Appendix IV

Feed Analysis Reports

ISOFLAVONE PROFILE

PRODUCT: **CERTIFIED RODENT DIET**
Code: 5002

Lot Number: JUN 24 02 1B 1

Isoflavone Profile

Total Daidzein (Aglycone Units)	145	ppm
Total Genistein (Aglycone Units)	161	ppm
Total Glycitein (Aglycone Units)	35	ppm
Total All Forms (Aglycone Units)	341	ppm

For additional information concerning the report contact the Quality Department at Richmond, In. (Angela Crutcher) 765-962-9561 ext. 229

For additional information concerning the analytical results contact Dr. Dorrance Haught at 314-768-4362.

ISOFLAVONE PROFILE

PRODUCT: CERTIFIED RODENT DIET
Code: 5002

Lot Number: JUN 24 02 1B 2

Isoflavone Profile

Total Daidzein (Aglycone Units)	146	ppm
Total Genistein (Aglycone Units)	163	ppm
Total Glycitein (Aglycone Units)	37	ppm
Total All Forms (Aglycone Units)	346	ppm

For additional information concerning the report contact the Quality Department at Richmond, In. (Angela Crutcher) 765-962-9561 ext. 229

For additional information concerning the analytical results contact Dr. Dorrance Haught at 314-768-4362.

ISOFLAVONE PROFILE

PRODUCT: CERTIFIED RODENT DIET
Code: 5002

Lot Number: JUN 24 02 1B 3

Isoflavone Profile

Total Daidzein (Aglycone Units)	149	ppm
Total Genistein (Aglycone Units)	166	ppm
Total Glycitein (Aglycone Units)	38	ppm
Total All Forms (Aglycone Units)	353	ppm

For additional information concerning the report contact the Quality Department at Richmond, In. (Angela Crutcher) 765-962-9561 ext. 229

For additional information concerning the analytical results contact Dr. Dorrance Haught at 314-768-4362.

PRODUCT: CERTIFIED RODENT DIET
Code: 5002 Lot Number: DEC 02 02 2B

SAMPLE: # 1

IFSP

Isoflavone profile, saponification

Daidzin	199	ppm
Daidzein	7.0	ppm
Total Daidzein Compounds	206	ppm
Genistin	219	ppm
Genistein	2.0	ppm
Total Genistein Compounds	221	ppm
Glycitin	52.0	ppm
Glycitein	2.0	ppm
Total Glycitein Compounds	54	ppm
Total Isoflavones	481	ppm
Daidzin (Aglycone Units)	122	ppm
Daidzein (Aglycone Units)	7.0	ppm
Total Daidzein (Aglycone Units)	129	ppm
Genistin (Aglycone Units)	137	ppm
Genistein (Aglycone Units)	2.0	ppm
Total Genistein (Aglycone Units)	139	ppm
Glycitin (Aglycone Units)	33.0	ppm
Glycitein (Aglycone Units)	2.0	ppm
Total Glycitein (Aglycone Units)	35.0	ppm
Total Isoflavones (Aglycone Units)	303	ppm

For additional information concerning the report contact the Quality Department at Richmond, In. (Virgil Strobel) 765-962-9561 ext. 225 (email - virgil_strobel@purina-mills.com)

For additional information concerning the analytical results contact Dr. Dorrance Haught at 314-768-4362. (email - dorrance_haught@purina-mills.com)

PRODUCT: CERTIFIED RODENT DIET
Code: 5002 Lot Number: DEC 02 02 2B

SAMPLE: # 2

IFSP

Isoflavone profile, saponification

Daidzin	191	ppm
Daidzein	7.0	ppm
Total Daidzein Compounds	198	ppm
Genistin	212	ppm
Genistein	3.0	ppm
Total Genistein Compounds	215	ppm
Glycitin	50.0	ppm
Glycitein	2.0	ppm
Total Glycitein Compounds	52	ppm
Total Isoflavones	465	ppm
Daidzin (Aglycone Units)	117	ppm
Daidzein (Aglycone Units)	7.0	ppm
Total Daidzein (Aglycone Units)	124	ppm
Genistin (Aglycone Units)	133	ppm
Genistein (Aglycone Units)	3.0	ppm
Total Genistein (Aglycone Units)	136	ppm
Glycitin (Aglycone Units)	32.0	ppm
Glycitein (Aglycone Units)	2.0	ppm
Total Glycitein (Aglycone Units)	34.0	ppm
Total Isoflavones (Aglycone Units)	294	ppm

For additional information concerning the report contact the Quality Department at Richmond, In. (Virgil Strobel) 765-962-9561 ext. 225 (email - virgil_strobel@purina-mills.com)

For additional information concerning the analytical results contact Dr. Dorrance Haught at 314-768-4362. (email - dorrance_haught@purina-mills.com)

PRODUCT: CERTIFIED RODENT DIET
Code: 5002 Lot Number: DEC 02 02 2B

SAMPLE: # 3

IFSP

Isoflavone profile, saponification

Daidzin	179	ppm
Daidzein	6.0	ppm
Total Daidzein Compounds	185	ppm
Genistin	197	ppm
Genistein	2.0	ppm
Total Genistein Compounds	199	ppm
Glycitin	46.0	ppm
Glycitein	2.0	ppm
Total Glycitein Compounds	48	ppm
Total Isoflavones	432	ppm
Daidzin (Aglycone Units)	109	ppm
Daidzein (Aglycone Units)	6.0	ppm
Total Daidzein (Aglycone Units)	115	ppm
Genistin (Aglycone Units)	123	ppm
Genistein (Aglycone Units)	2.0	ppm
Total Genistein (Aglycone Units)	125	ppm
Glycitin (Aglycone Units)	29.0	ppm
Glycitein (Aglycone Units)	2.0	ppm
Total Glycitein (Aglycone Units)	31.0	ppm
Total Isoflavones (Aglycone Units)	271	ppm

For additional information concerning the report contact the Quality Department at Richmond, In. (Virgil Strobel) 765-962-9561 ext. 225 (email - virgil_strobel@purina-mills.com)

For additional information concerning the analytical results contact Dr. Dorrance Haught at 314-768-4362. (email - dorrance_haught@purina-mills.com)

Certified Rodent Diet 5002*

DESCRIPTION

Certified Rodent Diet is a Constant Nutrition™ formulation that has yielded highly favorable results for the maintenance, growth and reproduction of rats and mice. It has been developed as a complete life-cycle diet that can also be used by breeders to assure animals do not develop undesirable tissue residues of contaminants. A sample of this product will have been assayed prior to shipment.

Features and Benefits

- Each package is assayed for environmental contaminants prior to shipment
- Preanalysis monitoring assures maximum diet control
- Fulfills GLP requirements

Product Forms Available

- Oval pellet, 10 mm x 16 mm x 25 mm length (3/8"x5/8"x1")
- Meal (ground pellets)

GUARANTEED ANALYSIS

Crude protein not less than	20.0%
Crude fat not less than	4.5%
Crude fiber not more than	5.5%
Ash not more than	7.0%
Added minerals not more than	2.5%

INGREDIENTS

Ground corn, dehulled soybean meal, ground wheat, fish meal, wheat middlings, brewers dried yeast, cane molasses, wheat germ, dried beet pulp, dehydrated alfalfa meal, ground oats, dried whey, ground soybean hulls, soybean oil, calcium carbonate, casein, salt, dicalcium phosphate, choline chloride, DL-methionine, cholecalciferol, vitamin A acetate, pyridoxine hydrochloride, dl-alpha tocopheryl acetate, thiamin mononitrate, nicotinic acid, calcium pantothenate, riboflavin, cyanocobalamin, folic acid, manganous oxide, zinc oxide, ferrous carbonate, copper sulfate, zinc sulfate, calcium iodate, cobalt carbonate.

FEEDING DIRECTIONS

Feed ad libitum to rodents. Plenty of fresh, clean water should be available to the animals at all times. Refer to the "Animal Care and Biological Values" section of this manual for detailed feeding directions.

Rats- All rats will eat varying amounts of feed depending on their genetic origin. Larger strains will eat between 15-30 grams per day. Smaller strains will eat between 12-15 grams per day. Feeders in rat cages should be designed to hold two to three days supply of feed at one time.

Mice-Adult mice will eat 4 to 5 grams of pelleted ration daily. Some of the larger strains may eat as much as 8 grams per day per animal. Feed should be available on a free choice basis in wire feeders above the floor of the cage.

Hamsters-Adults will eat 10 to 14 grams per day.

CHEMICAL COMPOSITION[1]

Nutrients[2]

Protein, %	**20.1**
Arginine, %	1.13
Cystine, %	0.27
Glycine, %	0.86
Histidine, %	0.49
Isoleucine, %	1.03
Leucine, %	1.58
Lysine, %	1.18
Methionine, %	0.43
Phenylalanine, %	0.88
Tyrosine, %	0.59
Threonine, %	0.78
Tryptophan, %	0.24
Valine, %	1.05
Serine, %	1.01
Aspartic Acid, %	2.19
Glutamic Acid, %	4.20
Alanine, %	1.24
Proline, %	1.47
Taurine, %	0.01
Fat (ether extract), %	**4.5**
Fat (acid hydrolysis), %	**5.1**
Cholesterol, ppm	150
Linoleic Acid, %	2.15
Linolenic Acid, %	0.16
Arachidonic Acid, %	<0.01
Omega-3 Fatty Acids, %	0.34
Total Saturated Fatty Acids, %	0.86
Total Monounsaturated Fatty Acids, %	1.14
Fiber (Crude), %	**4.6**
Neutral Detergent Fiber[3], %	13.8
Acid Detergent Fiber[4], %	5.9
Nitrogen-Free Extract (by difference), %	**55.0**
Starch, %	36.3
Glucose, %	0.25
Fructose, %	0.30
Sucrose, %	3.13
Lactose, %	1.11
Total Digestible Nutrients, %	**77.0**
Gross Energy, kcal/gm	**4.04**
Physiological Fuel Value[5], kcal/gm	**3.41**
Metabolizable Energy, kcal/gm	**3.10**

Minerals

Ash, %	**5.8**
Calcium, %	0.80
Phosphorus, %	0.60
Phosphorus (non-phytate), %	0.34
Potassium, %	0.86
Magnesium, %	0.21
Sulfur, %	0.25
Sodium, %	0.30
Chlorine, %	0.47
Fluorine, ppm	13
Iron, ppm	210
Zinc, ppm	76
Manganese, ppm	75
Copper, ppm	11
Cobalt, ppm	0.6
Iodine, ppm	0.77
Chromium, ppm	2.0
Selenium, ppm	0.25

Vitamins

Carotene, ppm	5.6
Vitamin K (as menadione),ppm	0.4
Thiamin Hydrochloride, ppm	16
Riboflavin, ppm	8.0
Niacin, ppm	95
Pantothenic Acid, ppm	17
Choline Chloride, ppm	1800
Folic Acid, ppm	4.0
Pyridoxine, ppm	6.0
Biotin, ppm	0.13
B_{12}, mcg/kg	20
Vitamin A, IU/gm	18
Vitamin D_3 (added), IU/gm	2.2
Vitamin E, IU/kg	66

Calories provided by:

Protein, %	23.585
Fat (ether extract), %	11.880
Carbohydrates, %	64.535

*Product Code

1. Based on the latest ingredient analysis information. Since nutrient composition of natural ingredients varies, analysis will differ accordingly.
2. Nutrients expressed as percent of ration except where otherwise indicated. Moisture content is assumed to be 10.0% for the purpose of calculations.
3. NDF = approximately cellulose, hemi-cellulose and lignin.
4. ADF = approximately cellulose and lignin.
5. Physiological Fuel Value (kcal/gm) = Sum of decimal fractions of protein, fat and carbo- hydrate (use Nitrogen Free Extract) x 4,9,4 kcal/gm respectively.

Appendix V

Protocol and Two Amendments

EPA Contract No.: 68-W-01-023 (Battelle Prime Contractor)
RTI Contract No.: 65U-08055.001.015.001 (male)
RTI Study Code: Rt02-ED03 5/20/02
RTI Master Protocol No.: RTI-831

TITLE: Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 Through 52/53

SPONSOR: Battelle Memorial Institute
505 King Avenue
Columbus, OH 43201-2693

TESTING FACILITY: RTI
Chemistry and Life Sciences
Center for Life Sciences and Toxicology
Post Office Box 12194
Research Triangle Park, NC 27709

PROPOSED STUDY IN-LIFE DATES: July 2002 - September 2002 (Component 1)
September 2002 - November 2002 (Component 2)

AMENDMENTS:

Number	Date	Section(s)	Page(s)
1	4/17/03	Approval Page, 2.1, 2.3	2, 7, 8
* ~~2~~	4/17/03	2.4.3, 2.4.4, 2.5.1	9, 10
* ~~3~~	4/17/03	2.5.3, 3.1, Table 1	11, 12, 13
* ~~4~~	4/17/03	3.2.3.2, 3.4, 3.6.2	15, 16, 17
* ~~5~~	4/17/03	3.6.3, 7.0, 8.0	18, 19, 20

* JDGeorge 6/26/03
Amendment numbers 2 through 5 crossed out to allow space to describe amendment 1
JDGeorge 6/26/03

APPROVED BY:

Rochelle W. Tyl, Ph.D., DABT — Date 5/21/02
Project Toxicologist
Center for Life Sciences and Toxicology
RTI

Julia D. George, Ph.D. — Date 5/20/02
Study Director
Center for Life Sciences and Toxicology
RTI

James P. Kariya — Date 5-24-02
Work Assignment Manager
Endocrine Disruptor Screening Program
U.S. EPA

David P. Houchens, Ph.D. — Date 5/22/02
Principal Investigator/Program Manager
Endocrine Disruptor Screening Program
Battelle Memorial Institute

L. Greg Schweer — Date 5-28-02
Project Officer
Endocrine Disruptor Screening Program
U.S. EPA

REVIEWED BY:

Doris J. Smith, B.S. — Date 5-20-2002
Quality Assurance Manager
RTI

Charles Lawrie — Date 5/22/02
Quality Assurance Manager
Battelle Memorial Institute

TABLE OF CONTENTS

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1.0 OBJECTIVE AND BACKGROUND

The objective of this study is to quantify the effects of environmental compounds on pubertal development and thyroid function in the intact juvenile/peripubertal male rat. This assay detects compounds that display antithyroid, estrogenic, androgenic, antiandrogenic [androgen receptor (AR) or steroid enzyme mediated] activity, or alter follicle stimulating hormone (FSH), luteinizing hormone (LH), prolactin, growth hormone (GH), or hypothalamic function.

The Food Quality Protection Act of 1996 required the EPA to develop and implement a screening program for determining the potential in humans for estrogenic (and anti-estrogenic) effects from pesticides. This program has been expanded on the advice of the Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC) to include androgenic (and anti-androgenic) effects and effects from thyroid-hormone (TH)-like (and anti-TH) substances.

The EDSTAC, assembled by the EPA in 1996, recommended the use of a female 20-day pubertal assay with thyroid to evaluate test materials for effects on the thyroid, hypothalamic-pituitary-gonadal (HPG) axis, aromatase and estrogens (and/or other test materials) that are only effective orally, or after a dosing duration longer than that used in the uterotrophic assay (EDSTAC Report, 1998, Vol. 1, Chapter 5, p. 5-26). EDSTAC also recommended, as an alternate assay to be evaluated, the male 20-day thyroid/pubertal assay in rodents (EDSTAC, 1998, Vol. 1, Chapter 5, p. 5-30).

The EDSTAC discussion on the usefulness of the male pubertal assay and its endpoints included the following:

> "This assay detects androgens and antiandrogens *in vivo* in a single stage apical test. "Puberty" is measured in male rats by determining age at PPS (preputial separation). Animals are dosed by gavage beginning one week before puberty (which occurs at about 40 days of age) and PPS is measured. Androgens will accelerate and antiandrogens and estrogens will delay PPS. The assay takes about 3 weeks, and allows for comprehensive assessment of the entire endocrine system in one study (10 per group, selected for uniform body weights to reduce variance). The animals are dosed daily, seven days a week, and examined daily for PPS. Dosing continues until 53 days of age; the males are then necropsied. The body, heart (thyroid), adrenal, testis, seminal vesicle plus coagulating glands (with fluid), ventral prostate, and levator ani plus bulbocavernosus muscles (as a unit) are weighed. The thyroid is retained for histopathology and serum is taken for T4, T3, and TSH. Testosterone, LH, prolactin, and dihydrotestosterone analyses are optional. These endpoints take several weeks to evaluate and are affected not only by estrogens but by environmental antiandrogens, drugs that affect the hypothalamic-pituitary axis (Hostetter and Piacsek, 1977; Ramaley and Phares, 1983), and by prenatal exposure to TCDD (Gray et al., 1995a; Bjerke and Peterson, 1994) or dioxin-like PCBs (Gray et al., 1995b). In contrast to these other mechanisms, only peripubertal estrogen administration accelerates this process in the female and delays it in the male. Preputial separation in the male rodent is easy to measure and this is not a terminal measure (Korenbrot et al., 1977).
>
> Age and weight at puberty, reproductive organ weights, and serum hormone levels can also be measured. Delays in male puberty results form exposure to both estrogenic and antiandrogenic

chemicals including methoxychlor (Gray et al., 1989), vinclozolin (Anderson et al., 1995a), and p,p'DDE (Kelce et al., 1995). Exposing weanling male rats to the antiandrogenic pesticides p,p'DDE or vinclozolin delays pubertal development in weanling male rats as indicated by delayed preputial separation and increased body weight (because they are older and larger) at puberty. In contrast to the delays associated with exposure to estrogenic substances, antiandrogens do not inhibit food consumption or retard growth (Anderson et al., 1995b). Antiandrogens cause a delay in preputial separation and affect a number of endocrine and morphological parameters including reduced seminal vesicle, ventral prostate, and epididymal weights. It is apparent that PPS is more sensitive than are organ weights in this assay. In addition, responses of the HPG are variable. In studies of vinclozolin, increases in serum LH were a sensitive response to this antiandrogen, whereas serum LH is not increased in males exposed to p,p'DDE during puberty (Kelce et al., 1997). Furthermore, a systematic review of the literature indicates that the sex accessory glands of the immature intact male rat are consistently more affected than in the adult intact male rat.

In summary, preputial separation and sex accessory gland weights are sensitive endpoints. However, a delay in preputial separation is not pathognomonic for antiandrogens. Pubertal alterations result from chemicals that disrupt hypothalamic-pituitary function (Huhtaniemi et al., 1986) and, for this reason, additional *in vivo* and *in vitro* tests are needed to identify the mechanism of action responsible for the pubertal alterations. For example, alterations of prolactin, growth hormone, gonadotrophin (LH and FSH) secretion, or hypothalamic lesions alter the rate of pubertal maturation in weanling rats.

As indicated above, the determination of the age at "puberty" in the male rat are endpoints that already have gained acceptance in the toxicology community. Preputial separation in the male is a required endpoint in the new EPA two-generation reproductive toxicity test guideline. In this regard, this assay would be easy to implement because these endpoints have been standardized and validated and PPS data are currently being collected under GLP conditions in most toxicology laboratories. In addition, PPS data are reported in many recently published developmental and reproductive toxicity studies (i.e., see studies from R.E. Peterson's, J. Ashby's, R. Chapin's and L.E. Gray's laboratories on dioxins, PCBs, antiandrogens, and xenoestrogens).

Sex accessory gland weights in intact adult male rats also can be affected directly or indirectly by toxicant exposure. The HPG axis in an intact animal is able to compensate for the action of antiandrogens by increasing hormone production, which counteracts the effect of the antiandrogen on the tract (Raynaud et al., 1984; Edgren, 1984; Hershberger, 1953)." (EDSTAC, 1998, Vol. 1, Chapter 5, pp. 5-30 through 5-32).

Based on the EDSTAC's recommendations, one of the assays that the EPA has proposed to validate as a potential alternative for other assays in the Tier 1 battery in an endocrine disruptor screening program is a male pubertal assay (see FR Vol. 63, No. 248, pp. 71541-71568, December 28, 1998). This assay is the most comprehensive assay in the proposed Tier 1 battery of assays, as it is capable of detecting substances that alter thyroid function, that are aromatase inhibitors, androgens, anti-androgens, and that are agents which interfere with the hypothalamus-pituitary-gonadal axis. Results from other shorter assays and/or with the use of ip injection as the route of administration, have also been reported (O'Connor et al., 1996, 1999).

EPA has already tested the response of the pubertal assays to a variety of chemicals, but at only one dose per chemical (Rocca and Borst, 2000; Rocca and Pepperl, 2000a,b,c). EPA is in

the process of testing the response of two chemicals (vinclozolin and methoxychlor) at multiple doses to determine the sensitivity of the assays to subtle effects of estrogens and antiandrogens.

Although the experiments that have been completed or are in progress are believed to be sufficient to demonstrate the usefulness of these pubertal assays for a wide variety of chemicals, EPA feels that additional multiple-dose studies across an array of chemicals will provide greater confidence in the reliability and relevance of the assays. Therefore, EPA has decided to test ten additional chemicals that have various modes of action. Some chemicals will be tested in only males, others will be tested only in females, and some will be tested in both sexes.

2.0 MATERIALS AND METHODS

2.1 TEST SUBSTANCES

2.1.1 Atrazine

CAS Number 1912-24-9

2.1.2 Propylthiouracil

CAS Number 51-52-5

2.1.3 Vinclozolin

CAS Number 50471-44-8

2.1.4 Linuron

CAS Number 330-55-2

2.1.5 p,p-DDE

CAS Number 72-55-9

2.1.6 Ketoconazole

CAS Number 65277-42-1

2.1.7 Methoxychlor

CAS Number 72-43-5

2.1.8 Finasteride

CAS Number 98319-26-7

2.1.9 Phenobarbital

CAS Number 50-06-6

NOTE: All additional information on the test chemicals (e.g., supplier, batch/lot number, purity, appearance, molecular formula, molecular weight, storage conditions of bulk chemical, and of dosing suspensions, etc.) will be added to the protocol by amendment.

2.2 CHEMICAL SAFETY AND HANDLING

See MSDSs of all chemicals in Attachment.

2.3 DOSE FORMULATION AND ANALYSIS

The dosing suspensions will be prepared at a frequency determined by stability tests performed prior to the start of the study. Suspensions will be prepared at Battelle Chemical Repository, Sequim, WA, and stored in wide-mouth, amber bottles. They will be shipped via 24-hour express delivery and logged into the Materials Handling Facility prior to transfer to the Reproductive and Developmental Toxicology Laboratory for dosing. The test materials will be suspended in stripped (α-tocopherol [Vitamin E] removed) Mazola® corn oil (CAS No. 8001-30-7), with the concentration determined by the following formula:

$$\text{Concentration (mg / ml)} = \frac{\text{Dose per time (mg / kg)}}{\text{Dosage volume per time (5.0 ml / kg)}}$$

An aliquot of each dose level per formulation will be analyzed by Battelle. The dosing bottles will be identified at RTI by a five-digit random number Rx code, and a color code. Personnel, other than the Laboratory Supervisor, Project Toxicologist, and Study Director, will not be informed of the test chemicals or formulation concentrations until all laboratory work is completed (i.e., the study technicians will be "blind" for chemical and dose). Aliquots from the dosing bottles will be collected on the first day of dosing (postnatal day [pnd] 23) and on the first pnd 30, 37, 44, and 51, and will be shipped to Battelle Chemical Repository, Sequim, WA, for analysis.

2.4 ANIMALS

2.4.1 Species and Supplier

The proposed test animals will be the Sprague Dawley Derived Outbred Albino Rat Crl:CD®(SD) IGS BR supplied by Charles River Laboratories, Inc., Raleigh, NC.

2.4.2 Live Animals and Species Justification

The use of live animals has been requested by the Sponsor. Alternative test systems are not available for the assessment of effects of chemicals on reproduction and development in intact mammals for determining the potential risk for humans from endocrine-mediated effects of pesticides and other chemicals. The Charles River CD® rat has been the subject of choice on reproductive and developmental toxicology contracts at RTI since 1976, and has been used for other reproductive toxicology studies with this test material. Large historical data bases for reproductive performance and prevalence of spontaneous malformations in control rats are available from studies conducted at RTI (currently based on over 300 control litters) as well as from the supplier (Charles River, 1988). This study does not unnecessarily duplicate any previous study.

2.4.3 Total Number, Age, and Weight

For the nine-group component of this study (Component 1; see Table 1), 25 timed-pregnant female rats (designated the F0 generation) will be purchased for this study, at ten to 12 weeks of age upon arrival. They will arrive at RTI on gestational day (gd) 14 (based on the vendor's designation of the day of insemination as gd 1), which is gd 13 (based on the performing laboratory's designation of the day of insemination as gd 0). One hundred thirty-five (135) offspring male rats, designated the F1 generation, will be placed on study at weaning (pnd 21), weighing approximately 48-55 grams (i.e., nine groups of 15 F1 weanling males each), for Component 1. For the 11-group component of this study (Component 2; see Table 1), 32 timed-pregnant female rats will be purchased, as described above, and 165 offspring male rats (11 groups of 15 F1 weanling males each) will go on study for Component 2.

2.4.4 Quality Control

The shipment of pregnant F0 females will be quarantined on arrival, and quality control evaluation will be initiated within one day after receipt. Within one day after receipt, two female rats will be chosen from the shipment, sacrificed, and blood collected for assessment of viral antibody status. Heat-inactivated serum will be sent to BioReliance (Rockville, MD) for their Level 1 Rat Antibody Screen. The viral screen will consist of evaluation for the presence of antibodies against the following: Toolan H-1 virus (H-1), Sendai virus, Pneumonia virus of mice (PVM), rat coronavirus/ sialodacryoadenitis (RCV/SDA), Parvo virus, Kilham rat virus (KRV), CAR Bacillus, and Mycoplasma pulmonis (*M. Pul.*). In addition, fecal samples from representative animals will be externally examined for intestinal parasites.

2.4.5 Sentinels

After the selection of F1 weanling study males, four unselected male rats (or, if necessary, one to four remaining females) will be randomly selected, eartagged, and designated as sentinels. They will be singly housed in the study room(s) with feed and water available *ad libitum* (as described below). They will be examined once daily by cageside observation for morbidity or mortality at the same time as the clinical observations or morbidity/mortality checks for the study animals. The clinical condition of sentinel animals will be recorded only in the event that an animal is moribund or found dead. If a sentinel animal is terminated moribund, blood will be collected at termination and serum samples frozen.

During the F1 male necropsies, the surviving sentinel males (and/or females) will be terminated, blood samples collected, and serum samples prepared. All sentinel serum samples will be submitted to BioReliance (Rockville, MD) for serological evaluation (see above section on Quality Control).

2.4.6 Quarantine

The initial F0 timed-pregnant females will be quarantined for approximately one week (gd 13-20), with the prior concurrence of the RTI Animal Research Facility (ARF) veterinarian. They will be observed daily for general health status and ability to adapt to the ARF husbandry conditions. They will be released from quarantine, if suitable for use (based on QC results), by the attending ARF veterinarian or his designate.

2.5 ANIMAL HUSBANDRY

2.5.1 Housing, Feed, and Water

During the quarantine period, animals will be randomly assigned to cages. Pregnant and lactating F0 females will be singly housed, and and F1 male postweanlings will be multiply or singly housed, as necessary, in solid-bottom, polycarbonate cages (8"x19"x10.5") fitted with stainless steel wire lids (Laboratory Products, Rochelle Park, NJ). Sani-Chip® cage bedding (P.J. Murphy, Forest Products, Inc., Montville, NJ) will be used in all cages. Pelleted feed (No. 5002 Purina Certified Rodent Chow®) and deionized water, produced at RTI from tap water from the Durham, NC water system, in plastic bottles with stainless steel sipper tubes, will be available *ad libitum* for the F0 females during quarantine, gestation and lactation, and for the retained F1 males. The water for the study breeder male animals is provided by an automatic watering system (Edstrom Industries, Inc., Waterford, WI); the parental females will also be on the automatic watering system during cohabitation. The analysis of the rodent chow for chemical composition and possible chemical contamination, and analysis of Durham City water will be provided by the suppliers and maintained in the study records. It is anticipated that contaminant levels will be below certified levels for both feed and water and will not affect the design, conduct, or conclusions of this study. In addition, each lot number of Purina 5002 feed used will be analyzed by the supplier for concentrations of the phytoestrogens genistein, daidzein, and glycitein. An aliquot of each lot number will be retained frozen for possible future analytical chemistry. The "metabolizable energy content" of the feed (label value) will also be recorded and reported. Rat chow will be stored at approximately 60-70°F, and the period of use will not exceed six months from the milling date. At all times, animals will be housed, handled, and used according to the NRC Guide (NRC, 1996).

2.5.2 Environmental Conditions

Environmental conditions in the ARF will be continuously monitored, recorded, and controlled during the course of the study by an automated system (Siebe/Barber-Colman Network 8000 System with Version 4.4.1 Signal® software (Siebe Environmental Controls (SEC)/ Barber-Colman Company, Loves Park, IL). Animal rooms used for this study will be maintained on a 14:10 hour light:dark cycle. Target conditions for temperature and relative humidity in the animal

rooms will be between 64-79°F (18-26°C) and 30-70%, respectively, with 10-15 air changes per hour (NRC, 1996). Temperature and/or relative humidity excursions will be documented in the study records and the final report.

2.5.3 Animal Identification

All F0 maternal rats will be individually identified by ear tag after arrival at RTI. All selected study weanling F1 males will also be uniquely identified by eartag at weaning, as well as receiving a female study number. All data generated during the course of this study will be tracked by these numbers.

2.5.4 Limitation of Discomfort

Some postweanling toxicity may be caused by exposure at the high doses of each test material. Discomfort or injury to animals will be limited, in that if any animal becomes severely debilitated or moribund, it will be humanely terminated by CO_2 inhalation. All necropsies will be performed after terminal CO_2 asphyxiation. F1 pnd 4 culled pups will be euthanized by decapitation and discarded.

3.0 EXPERIMENTAL DESIGN

3.1 STUDY DESIGN, TEST CHEMICALS, AND DOSE SELECTION

The study will be conducted in two components. Component 1 will consist of two dose groups per test material (and four test materials) and one vehicle control group. Component 2 will consist of two dose groups per test material (and five test materials) and one vehicle control group. Each group will be comprised of 15 weight-matched F1 male weanlings for each of the two components of this study. The F1 study males will be dosed by gavage once daily for 31-32 consecutive days (pnd 22 to pnd 52 or 53). Table 1 presents the study design and target doses of the test chemicals. A graphical representation of the study design is presented in Figure 1 below.

The U.S. EPA selected the nine test chemicals for evaluation and selected the low and high target doses (in mg/kg/day) for each of them (Table 1). The nine test chemicals and their target/mechanism of action are as follows: (1) atrazine (affects the hypothalamus-pituitary axis in female rats and ovulation); (2) propylthiouracil (affects the thyroid directly, causing hypothyroidism); (3) vinclozolin (metabolites M1 and M2 act as anti-androgen; competitive binding to androgen receptor; M1 also binds weakly to the rat progesterone receptor); (4) linuron (anti-androgen; competitive binding to androgen receptor); (5) p,p-DDE (stable metabolite of DDT; anti-androgen through competitive binding to the androgen receptor); (6) ketoconazole (inhibits steroidogenesis in both sexes); (7) methoxychlor (a xeno-estrogen through α-estrogen receptor, anti-estrogen through β-estrogen receptor and an anti-androgen through androgen receptor mediated mechanism); (8) finasteride (a inhibitor of a 5α-reductase which catalyzes the conversion of testosterone to its potent metabolite, dihydrotestosterone [DHT]); and (9) phenobarbital (induces P450 isoforms predominantly in the liver, accelerates metabolism of endogenous hormones and exogenous xenobiotics).

Tentative Study Dates[a] (to be added to the protocol by amendment)

F0 timed-pregnant females arrive at RTI:
Parturition of F1 offspring (pnd 0):
Weaning of F1 offspring (pnd 21):
Sacrifice of F0 dams:
Dosing (pnd 23 - pnd 52/53):
Sacrifice of F1 males (on pnd 52 or 53):
Submission of nonaudited draft final report:
Submission of audited draft final report:

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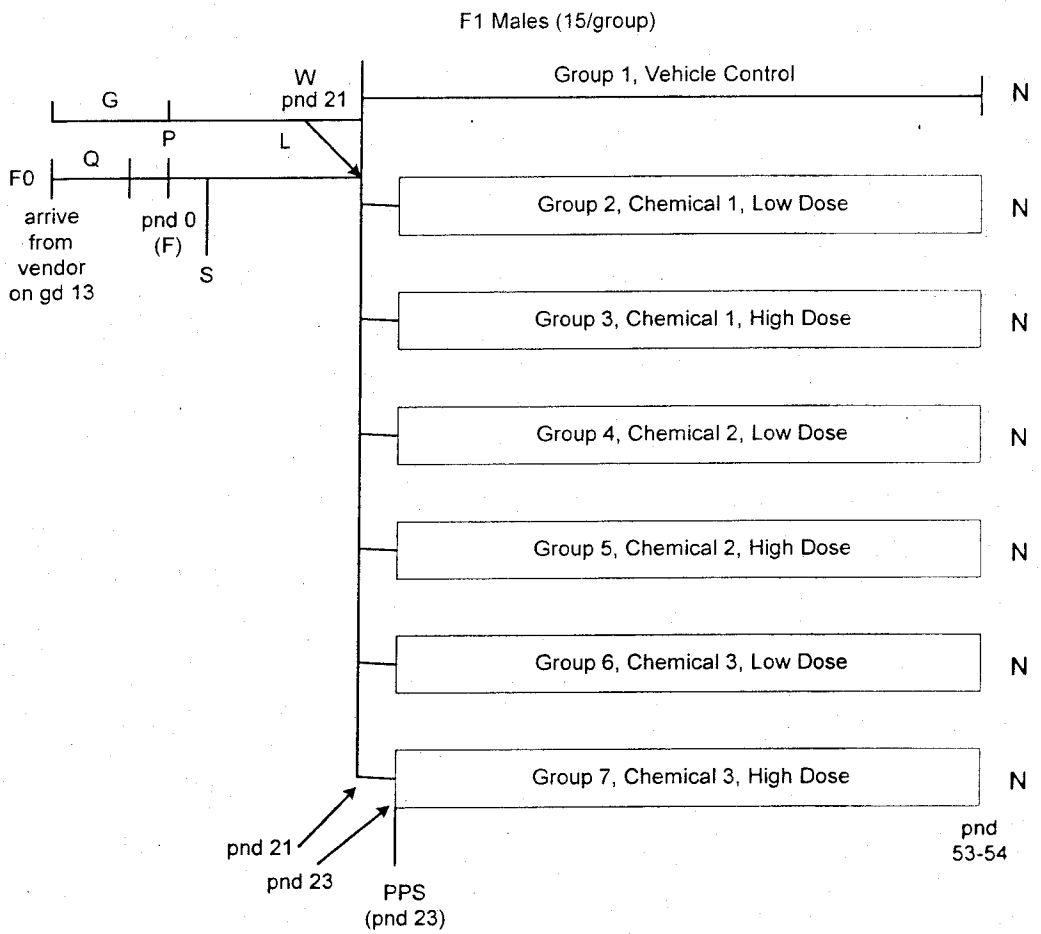
[a] The end dates are tentative and will depend on the duration of gestation and lactation of the F0 dams with F1 offspring.

Table 1. Study Design and Target Doses

Group No.	No. F1 Males	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)	Dose Volume (ml/kg)
			COMPONENT 1		
1	15	–[a]	0	0.0	5.0
2	15	Atrazine	75	15.0	5.0
3	15		150	30.0	5.0
4	15	Propylthiouracil	2	0.4	5.0
5	15		25	5.0	5.0
6	15	Vinclozolin	30	6.0	5.0
5	15		100	20.0	5.0
8	15	Linuron	50	10.0	5.0
9	15		100	20.0	5.0
			COMPONENT 2		
10	15	p,p'DDE	50	10.0	5.0
11	15		100	20.0	5.0
12	15	Ketoconazole	50	10.0	5.0
13	15		100	20.0	5.0
14	15	Methoxychlor	25	5.0	5.0
15	15		50	10.0	5.0
16	15	Finasteride	25	5.0	5.0
17	15		50	10.0	5.0
18	15	Phenobarbital	50	10.0	5.0
19	15		100	20.0	5.0
10	15	–[a]	0	0.0	5.0

[a] stripped corn oil, vehicle control



KEY:

——— No exposures to F0 dams or F1 offspring during gestation or lactation

▭ Direct once daily gavage dosing of F1 males beginning on pnd 23 (see text)

Q = Quarantine (seven days, gd 13-20)

G = Gestation

P = Parturition (pnd 0)

L = Lactation

W = Wean (pnd 21) F1 pups; euthanize and discard F0 dams

F = Foster pups, if necessary, to maximize retention of F1 male pups

S = Standardize litters to ten with maximum number of F1 male pups (discard culled pups)

PPS = Acquisition of preputial separation (evaluation will begin on pnd 23)

N = Necropsy (see text)

Figure 1. Study Design for Male Pubertal Assay

3.2 F0 DAMS AND F1 LITTERS PRIOR TO WEANING

3.2.1 F0 Maternal Parturition and Lactation

Beginning on gd 20, each female will be examined twice daily (a.m. and p.m.) for evidence of littering. Females who are littering at morning and afternoon checks will have this information recorded on the gestational sheet. Signs of dystocia or other signs of difficulty at parturition will be recorded. Dams that have not produced a litter by calculated gd 26 will be euthanized by CO_2 and discarded. Any dams whose whole litters are born dead or die prior to pnd 21 will be sacrificed, and the number of uterine implantation scars will be recorded.

3.2.2 Final Disposition of F0 Females

On pnd 21 of each F1 litter, each F0 dam will either be euthanized by CO_2 asphyxiation, and the carcass discarded, or will be transferred out of this study and used for training purposes in the RTI ARF. Final disposition of each animal will be clearly documented in the study records.

3.2.3 F1 Progeny

3.2.3.1 Mortality, Body Weights, and Clinical Observations

All pups will be counted, sexed, weighed, and examined as soon as possible on the day of birth (designated as pnd 0) to determine the number of viable and stillborn members of each litter. Thereafter, litters will be evaluated for survival, sex, gross observations, and body weights on pnd 4, 7, 14, and 21. Any pup which appears moribund or dies during lactation will be necropsied, when possible, to investigate the cause of death and discarded. No organs will be weighed or saved.

3.2.3.2 Standardization of Litter Sizes

On pnd 4, the size of each litter will be adjusted to ten pups, maximizing the number of male pups retained. Natural litters with ten or fewer pups will not be culled. If necessary, F1 male pups from litters with more than six males will be fostered to litters containing fewer than six males on pnd 4. All culled pups will be sacrificed by decapitation. The F0 dams will be allowed to rear their remaining F1 young to pnd 21. On pnd 21, each litter will be weaned.

3.3 SELECTION OF F1 WEANLING MALES

When each F1 litter has reached pnd 21, the F1 males for each pnd 21 (wean) date will be weight ranked across litters (outliers, i.e., heaviest and lightest pups, will be eliminated from selection). The selected males will then be eartagged and distributed across the seven groups by stratified randomization (e.g., one of the seven heaviest selected males will go into each of the seven treatment groups, etc.). Of the remaining F1 males, four will be eartagged and selected as sentinels. If not enough unselected males are available, then the remaining F1 females will be used as sentinels (to obtain a total of four); see Section 2.4.5.

3.4 TREATMENT OF F1 WEANLING MALES

Beginning on pnd 23, each F1 male will be dosed with one of the test materials at one of the dose levels or the vehicle control (corn oil for all chemicals). Each animal will be weighed every other day prior to treatment and the body weight recorded. Treatments will be administered daily by oral gavage in 5.0 ml corn oil/kg body weight from pnd 23 and continuing through pnd 52/53. This duration of treatment is unnecessary to detect androgenic chemicals but is required for the detection of pubertal delay and antithyroid effects. Gavage dosing will use an 18-gauge gavage needle (1 inch length with 2.25 mm ball) and a 1 cc glass (disposable) tuberculin syringe for each treatment group. Xenobiotics will be administered in corn oil vehicle at a dosing volume of 5.0 ml/kg body weight at 0700-1000 hours daily. The treatments will be administered on a mg/kg body weight basis, adjusted based on the most recent body weight, and the volume of the dose administered will be recorded each day. It is important that any dosing solutions/suspensions be well mixed to keep the chemical in suspension prior to and throughout dosing.

3.5 OBSERVATION OF F1 WEANLING MALES

3.5.1 Clinical Observations

Clinical observations of F1 male study animals will be documented at least once daily on pnd 21 and 22 (prior to dosing period) and at least twice daily, at dosing and one to two hours postdosing, throughout the dosing period (pnd 23 through pnd 52 or 53). The examining technicians will be unaware of the test materials or of dosage levels. Observations will be made for (but not limited to):

a. Any response with respect to body position, activity, coordination, or gait
b. Any unusual behavior such as head flicking, compulsive biting or licking, circling, etc.
c. The presence of:
    1. Convulsions, tremors, or fasciculations
    2. Increased salivation
    3. Increased lacrimation or red-colored tears (chromodacryorrhea)
    4. Increased or decreased urination or defecation (including diarrhea)
    5. Piloerection
    6. Mydriasis or miosis (enlarged or constricted pupils)
    7. Unusual respirations (fast, slow, labored, audible, gasping, or retching)
    8. Vocalization

3.5.2 F1 Weanling Male Body Weights

All F1 males will be weighed in the morning on pnd 21 and 22, and every day in the morning during the dosing period on pnd 23 through pnd 52/53, for adjustment of dosing volume based on the most recent body weight. Daily body weights will be reported and statistically analyzed. F1 male weight gains will be calculated and analyzed for pnd 21-23, 23-30, 30-37, 37-44, 44-51, 51-52/53, and 23-52/53 (treatment period). F1 male body weights will also be recorded on the day of acquisition of preputial separation (see Section 3.5.4).

3.5.3 F1 Weanling Male Feed Consumption

Feed consumption for the individually-housed F1 weanling males will be recorded daily and reported as g/day and as g/kg body weight/day.

3.5.4 Acquisition of Preputial Separation

Beginning on pnd 23, each F1 study male will be examined daily for preputial separation. The appearance of partial and complete preputial separation or a persistent thread of tissue between the glans and prepuce should all be recorded if and when they occur. In addition, the body weight at complete preputial separation should be recorded. However, if a sufficient number of animals within any treatment group show persistent threads for greater than three days, a separate analysis should be conducted using the age at which the thread was first observed.

3.6 NECROPSY OF F1 OFFSPRING MALES

3.6.1 Terminal Blood Collection

At scheduled necropsy of the F1 males, after terminal anesthesia (CO_2 asphyxiation), the males will be weighed and the maximum amount of blood will be taken by external cardiac puncture and placed in a labeled tube. The blood will be allowed to clot and centrifuged under refrigeration at approximately 1400 x g for approximately ten minutes. The resulting serum will be subdivided into two aliquots and frozen at approximately -20°C:

a. One milliliter from each animal for analysis of thyroxine (T4) and thyroid stimulating hormone (TSH) at RTI.

b. Remaining serum from each animal shipped frozen, for possible subsequent analyses, to:

Ralph L. Cooper, Ph.D.
Chief, Endocrinology Branch, MD-72
RTD, NHEERL, US EPA
Research Triangle Park, NC 27711
Cooper.ralph@epa.gov
Phone: 919-541-4084 Fax: 919-541-5138

3.6.2 Gross Necropsy and Organ Weights

Each F1 male offspring, after blood is collected (see Section 3.7.1), will be subjected to a gross necropsy. The thoracic and abdominal organs and cavities will be examined and any abnormalities documented. The following organs will be dissected out and weighed: paired testes, paired epididymides, prostate (intact and separated into ventral and dorsolateral lobes), seminal vesicles with coagulating glands (and fluid), levator ani plus bulbcavernosus muscle complex, liver, paired kidneys, adrenal glands (paired), pituitary, and thyroid (taken with attached portion of trachea, weighed after fixation and removal of the tracheal portion).

All organs will be weighed to the nearest 0.1 mg. Adrenal and pituitary glands will be weighed immediately (to minimize drying out of tissues). The thyroid will be weighed after fixation and removal of the attached trachea.

During necropsy, care must be taken to remove mesenteric fat with small surgical iris scissors from these tissues such that the fluid in the sex accessory glands is retained. Small tissues such as the adrenals, as well as tissues that contain fluid, should be weighed immediately to prevent partial drying prior to weighing.

3.6.3 Histology and Pathology

One testis, one epididymis, and the thyroid with attached portion of trachea from each F1 male will be placed in Bouin's fixative for 24 hours (then the trachea removed from the thyroid), after which they will be rinsed and stored in 70% alcohol until embedded in paraffin. They will then be sectioned at 3-5 microns and stained with hematoxylin and eosin (H and E) for subsequent histological evaluations. Optional tissues for histopathology include the liver, paired kidneys, adrenal glands (paired), and pituitary, as indicated by altered organ weight (change of "significant magnitude"), which will be processed as above. Stained sections will be evaluated by a Board Certified veterinary pathologist for pathologic abnormalities and potential treatment-related effects. Thyroids should be evaluated for morphologic changes such as altered follicular epithelial height, the relative number and staining characteristics of colloid, the extent of thyroid vascular supply, and the density, size, and shape of the thyroid follicles. The one testis and epididymis per male will be evaluated for spermatogenesis, spermiogenesis, status of seminiferous tubules in the testis, and sperm in the epididymis, as well as the structural integrity of these organs.

4.0 STATISTICAL ANALYSES

All data for a single chemical (two doses) and concurrent vehicle control group (weaning body weight, body weights and weight gains, age and weight at preputial separation, body and organ weights at necropsy, and serum hormones) will be analyzed using either parametric ANOVA under the standard assumptions or robust regression methods (Zeger and Liang, 1986; Royall, 1986; Huber, 1967) which do not assume homogeneity of variance or normality. The homogeneity of variance assumption will be examined via Levene's test (Levene, 1960). If Levene's test indicates lack of homogeneity of variance ($p<0.05$), robust regression methods will be used to test all treatment effects. The robust regression methods use variance estimators that make no assumptions regarding homogeneity of variance or normality of the data. They will be used to test for linear trends across dose as well as overall treatment group differences (via Wald chi-square tests). Significant overall treatment effects will be followed by single degree-of-freedom *t*-tests for exposed vs. control group comparisons, if the overall treatment effect is significant. If Levene's test does not reject the hypothesis of homogeneous variances, standard ANOVA techniques will be applied for comparing the treatment groups. The GLM procedure in SAS® Version 6 (SAS Institute, Inc., 1989a,b; 1990a,b,c; 1996; 1997) or 8 (SAS Institute, Inc.,

1999a,b,c,d,e; 2000) will be used to test for linear trend, evaluate the overall effect of treatment and, when a significant treatment effect is present, to compare each exposed group to control via Dunnett's Test (Dunnett, 1955, 1964). Standard ANOVA methods, as well as Levene's Test, are available in the GLM procedure of SAS®, and the robust regression methods are available in the REGRESS procedure of SUDAAN® Release 7.5.4 (Shah et al., 1997) or Release 8.0 (RTI, 2001). Organ weights will also be analyzed by Analysis of Covariance (ANCOVA) using the intital body weight (at assignment to treatment groups) and body weight at necropsy as the covariates. When statistically significant effects are observed, treatment means will be examined further using LSMeans.

The unit of comparison will be the weanling F1 male offspring on study.

A test for statistical outliers will be performed in the UNIVARIATE procedure of SAS® Version 6 (SAS Institute, Inc., 1989a,b; 1990a,b,c; 1996; 1997) or 8 (SAS Institute, Inc., 1999a,b,c,d,e; 2000) on F1 male body and organ weights. If examination of pertinent study data do not provide a plausible biologically sound reason for inclusion of the data flagged as "outlier," the data will be excluded from summarization and analysis and will be designated as outliers. For all statistical tests, $p \leq 0.05$ (one- or two-tailed) will be used as the criterion for significance.

5.0 RETENTION OF SPECIMENS AND RECORDS

All specimens and records which remain the responsibility of RTI will be retained in the RTI archives for two years at the performing laboratory's expense. Beyond two years, continued retention will be at additional cost to the Sponsor.

6.0 QUALITY CONTROL/QUALITY ASSURANCE PROCEDURES

Quality control (QC) and quality assurance (QA) procedures will follow those outlined in the Quality Assurance Project Plan (QAPP) prepared for this study.

7.0 REPORTING

An executive summary will be prepared describing the number and strain of rats used in the study, the doses and chemicals tested, and the effects with levels of statistical significance for all endpoints. Electronic and hard copies of spreadsheets containing the raw data from all animals will be provided for each endpoint. In addition, the spreadsheet should include treatment means, standard deviation, standard error, coefficient of variation, and sample number below each endpoint. Data presented should include animal number and treatment, block and day of necropsy (if study conducted in blocks or animals killed on pnd 52 and 53), age and weight at preputial separation, body weights at weaning, organ and body weights at necropsy, body weight change from pnd 23 to necropsy, and serum T4 and TSH. A data summary table containing the

mean, standard deviation, standard error, coefficient of variation, and sample size for each treatment group should be provided for all endpoints. Organ weights may be presented after covariance adjustment for necropsy body weight, but this should not replace presentation of the unadjusted data. Summaries of any histopathologic findings with photomicrographs of significant observations will also be provided.

8.0 PERSONNEL

Study Director:	Julia D. George, Ph.D.
Project Toxicologist:	Rochelle W. Tyl, Ph.D., DABT
ARF Veterinarian:	Donald B. Feldman, D.V.M., ACLAM
ARF Manager:	Frank N. Ali, M.B.A., RLATG, ILAM
Laboratory Supervisor:	Melissa C. Marr, B.A., RLATG
Data Analyst and Reproductive Toxicity Supervisor:	Christina B. Myers, M.S.
Statistical Advisor:	Gayle S. Bieler, M.S.
Research Data Entry Assistant:	Timothy W. Wiley, B.S.
Research Biologist:	William R. Ross, B.A.
Biologists:	Vickie I. Wilson Lawson B. Pelletier, RVMT, LAT
Biological Laboratory Assistants:	Marian V. Rieth, RVMT Malcolm D. Crews, ALAT Robin T. Krebs, ALAS
Endocrinology:	Patricia A. Fail, Ph.D. Carol S. Sloan, M.S. Kristi D. Vick, B.S.
Quality Assurance:	Doris J. Smith, B.S., Manager Celia D. Keller, M.S. Patricia D. Hall Marcia D. Phillips, M.S.

D. Denise Rowe, M.L.S.
Tiffany M. Kennedy, B.S.
Erica D. Shinauld, B.S.

Histology: Tsai-Ying Chang, B.S. HT-ASCP

Pathology: John C. Seely, D.V.M., ACVP (EPL, Inc.)

Additional study team members to be determined.

9.0 STUDY RECORDS TO BE MAINTAINED

Protocol and any Amendments
List of any Protocol Deviations
List of Standard Operating Procedures
Animal Requisition and Receipt Records
Quarantine Records
Temperature and Humidity Records for the Animal Room(s)
Animal Research Facility Room Log(s)
Durham City Water Analysis (analyzed monthly, reported annually)
Feed Type, Source, Lot Number, Dates Used, Certification, Analytical Results
Dosage Code Records Containing Five-Digit Rx Code, Color Code, and Concentration
F0 Mating Records from Vendor
F0 Maternal Gestational and Lactational Records
F0 Disposition Records
Dose Formulation Receipt and Use Records
F1 Male Distribution into Groups
F1 Male Dosing Forms
F1 Male Postwean Dosing Period: Body Weights
Clinical Signs
Acquisition of Preputial Separation

F1 Male Necropsy Records: Body weight, organ weights, gross observations, required (and optional, if done) organ histopathology, TSH and T4 serum levels

Statistical Analysis Records

Histopathology Report

Serum Thyroid Hormone Analyses (T4, TSH)

Correspondence

10.0 REFERENCES

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ATTACHMENT

Material Safety Data Sheets (MSDSs)

Atrazine	CAS No. 1912-24-9
Propylthiouracil	CAS No. 51-52-5
Vinclozolin	CAS No. 50471-44-8
Linuron	CAS No. 330-55-2
p,p-DDE	CAS No. 72-55-9
Ketoconazole	CAS No. 65277-42-1
Methoxychlor	CAS No. 72-43-5
Finasteride	CAS No. 98319-26-7
Phenobarbital	CAS No. 50-06-6

CHEM SERVICE -- PS-380 ATRAZINE, 99.5% PURE - REFERENCE STANDARD
MATERIAL SAFETY DATA SHEET
NSN: 681000F018378
Manufacturer's CAGE: 8Y898
Part No. Indicator: A
Part Number/Trade Name: PS-380 ATRAZINE, 99.5% PURE

General Information

Item Name: REFERENCE STANDARD
Company's Name: CHEM SERVICE INC
Company's P. O. Box: 3108
Company's City: WEST CHESTER
Company's State: PA
Company's Zip Code: 19381
Company's Emerg Ph #: (215) 386-2100
Company's Info Ph #: (215) 692-3026
Record No. For Safety Entry: 001
Tot Safety Entries This Stk#: 001
Date MSDS Prepared: 10JUL90
Safety Data Review Date: 03SEP90
Preparer's Company: CHEM SERVICE INC
Preparer's City: WEST CHESTER
Preparer's State: PA
Preparer's Zip Code: 19381
MSDS Serial Number: BKXTW

Ingredients/Identity Information

Proprietary: NO
Ingredient: ATRAZINE
Ingredient Sequence Number: 01
Percent: 99.5%
NIOSH (RTECS) Number: XY5600000
CAS Number: 1912-24-9
OSHA PEL: 5 MG/M3
ACGIH TLV: 5 MG/M3; 9192

Physical/Chemical Characteristics

Appearance And Odor: COLORLESS, CRYSTALLINE SOLID
Melting Point: 347-350.6F
Vapor Pressure (MM Hg/70 F): 7
Vapor Density (Air=1): 1.187
Solubility In Water: INSOLUBLE

Fire and Explosion Hazard Data

Extinguishing Media: CO2, DRY CHEMICAL POWDER OR SPRAY.

Reactivity Data

Stability: YES
Cond To Avoid (Stability): SENSITIVE TO HEAT
Hazardous Decomp Products: DECOMPOSES UNDER ALKALINE & ACIDIC CONDITIONS.
Hazardous Poly Occur: NO

Health Hazard Data

LD50-LC50 Mixture: LD50 (RAT OR MOUSE): 1750 MG/KG.
Route Of Entry - Inhalation: YES
Route Of Entry - Skin: YES
Route Of Entry - Ingestion: YES
Health Haz Acute And Chronic: EYES: IRRITATION & SEVERE INFLAMMATION. SKIN: IRRITATION & HARMFUL IF ABSORBED. INHALATION: MUCOUS MEMBRANE & RESPIRATORY TRACT IRRITATION, HARMFUL & SWELLING OF ADJOINING EYE TISSUES. INGESTION: HARMFUL.
Carcinogenicity - NTP: NO
Carcinogenicity - IARC: NO
Carcinogenicity - OSHA: NO
Explanation Carcinogenicity: NONE
IRRITATION & HARMFUL IF ABSORBED. INHALATION: MUCOUS MEMBRANE & RESPIRATORY HARMFUL.
Emergency/First Aid Proc: EYES/SKIN: FLUSH W/WATER FOR 15-20 MINS. IF NO BURNS HAVE OCCURED-USE SOAP & WATER TO CLEANSE SKIN. INHALATION: REMOVE TO FRESH AIR. ADMINISTER OXYGEN IF BREATHING DIFFICULTY. ADMINISTER CPR IF INDUCE VOMITING. DON'T ADMINISTER LIQUIDS/INDUCE VOMITING TO AN UNCONSCIOUS/CONVULSING PERSON. OBTAIN MEDICAL ATTEN. (SEE SUPP.)

Precautions for Safe Handling and Use

Steps If Matl Released/Spill: EVACUATE AREA. WEAR APPROPRIATE EQUIPMENT. VENTILATE AREA. SWEEP UP & PLACE IN AN APPROPRIATE CONTAINER. WASH CONTAMINATED SURFACES TO REMOVE ANY RESIDUES.
Waste Disposal Method: BURN IN A CHEMICAL INCINERATOR EQUIPPED W/AN AFTERBURNER & SCRUBBER. DISPOSE OF IN ACCORDANCE W/FEDERAL, STATE, & LOCAL REGULATIONS.
Precautions-Handling/Storing: KEEP CLOSED IN A COOL DRY PLACE. STORE ONLY W/COMPATIBLE CHEMICALS. FOR LABORATORY USE ONLY. DON'T WEAR CONTACT LENSES.
Other Precautions: DON'T USE AS DRUGS, COSMETICS, AGRICULTURAL OR PESTICIDAL PRODUCTS, FOOD ADDITIVES OR AS HOUSEHOLD CHEMICALS. AVOID DIRECT PHYSICAL CONTACT. AVOID CONTACT W/SKIN, EYES & CLOTHING.

Control Measures

Respiratory Protection: USE APPROPRIATE OSHA/MSHA APPROVED SAFETY

EQUIPMENT.
Ventilation: HANDLE ONLY IN A HOOD
Protective Gloves: AS REQUIRED
Eye Protection: EYE SHIELDS
Work Hygienic Practices: REMOVE/WASH CONTAMINATED CLOTHING BEFORE REUSE.
ONLY TRAINED PERSONNEL SHOULD HANDLE THIS CHEMICAL OR ITS CONTAINER.
Suppl. Safety & Health Data: FIRST AID: IF PATIENT IS VOMITING, WATCH CLOSELY TO MAKE SURE AIRWAY DOESN'T BECOME OBSTRUCTED BY VOMIT. OBTAIN MEDICAL ATTENTION IN ALL CASES.

Transportation Data

Disposal Data

Label Data

Label Required: YES
Label Status: G
Common Name: PS-380 ATRAZINE, 99.5% PURE
IRRITATION & HARMFUL IF ABSORBED. INHALATION: MUCOUS MEMBRANE & RESPIRATORY HARMFUL. EYES: IRRITATION & SEVERE INFLAMMATION. SKIN: IRRITATION & HARMFUL IF ABSORBED. INHALATION: MUCOUS MEMBRANE & RESPIRATORY TRACT IRRITATION, HARMFUL & SWELLING OF ADJOINING EYE TISSUES. INGESTION: HARMFUL.
Label Name: CHEM SERVICE INC
Label P.O. Box: 3108
Label City: WEST CHESTER
Label State: PA
Label Zip Code: 19381
Label Emergency Number: (215) 386-2100

NTP CHEMICAL REPOSITORY
6-N-PROPYL-2-THIOURACIL

-IDENTIFIERS
==========

*CATALOG ID NUMBER: 001351

*CAS NUMBER: 51-52-5

*BASE CHEMICAL NAME: PROPYLTHIOURACIL,6-N-,2-

*PRIMARY NAME: 6-N-PROPYL-2-THIOURACIL

*CHEMICAL FORMULA: C7H10N2OS

*STRUCTURAL FORMULA: Not printable

*WLN: T6MYMVJ BUS F3

*SYNONYMS:
4-HYDROXY-2-MERCAPTO-6-PROPYLPYRIMIDINE
PROCASIL
PROPACIL
PROPYCIL
6-PROPYL-2-THIO-2,4(1H,3H)PYRIMIDINEDIONE
PROPYLTHIOURACIL
6-PROPYL-2-THIOURACIL
6-PROPYLTHIOURACIL
PROTHYRAN
PTU
THYREOSTAT PROPYL-THYRACIL
PROTHIURONE
PROTHYCIL
PROTIURAL
PROPYL-THIORIST
PROPYLTHIORIT
THIURAGYL
PROTHIUCIL
PTU(THYREOSTATIC)
URACIL, 6-PROPYL-2-THIO-
2-MERCAPTO-6-PROPYLPYRIMID-4-ONE
2,3-DIHYDRO-6-PROPYL-2-THIOXO-4(1H)-PYRIMIDINONE
THYREOSTAT II
T 72
4(1H)-PYRIMIDINONE,2,3-DIHYDRO-6-PROPYL-2-THIOXO-

-PHYSICAL CHEMICAL DATA

*PHYSICAL DESCRIPTION: LITERATURE: White crystalline powder of starch-like appearance
REPOSITORY: White powder

*MOLECULAR WEIGHT: 170.23

*SPECIFIC GRAVITY: Not available

*DENSITY: Not available

*MP (DEG C): 219-221 C [031,042,315,395]

*BP (DEG C): Not available

*SOLUBILITIES:
WATER : <1 mg/mL @ 20 C (RAD)
DMSO : >=100 mg/mL @ 20 C (RAD)
95% ETHANOL : <1 mg/mL @ 20 C (RAD)
METHANOL : 10-50 mg/mL @ 19 C (RAD)
ACETONE : <1 mg/mL @ 20 C (RAD)
TOLUENE : <1 mg/mL @ 19 C (RAD)

OTHER SOLVENTS:
Boiling water: 1 part/100 parts [315,395]
Ether: Practically insoluble [031,042,315,395]
Ammonia (aqueous solutions): Freely soluble [031,062,315,395]
Alkali hydroxides (aqueous solutions): Freely soluble [031,051,062,205]
Chloroform: Practically insoluble [031,042,205,395]
Benzene: Practically insoluble [031,042,315,395]
Alcohol: 1 part/60 parts [295]

*VOLATILITY:
Vapor pressure: Not available
Vapor density : Not available

*FLAMMABILITY(FLASH POINT):
Flash point data for this chemical are not available; however it is probably combustible. Fires involving this material can be controlled with a dry chemical, carbon dioxide or Halon extinguisher.

*UEL: Not available LEL: Not available

*REACTIVITY:
This compound is incompatible with strong oxidizers, strong acids and strong bases [269]. It forms complexes with divalent metals [051,072,315,395]. It also reacts with sulphhydryl-oxidizing agents [051,072,395].

*STABILITY:
This chemical is sensitive to light [051,062,072,315]. It may be sensitive to prolonged exposure to air [455]. Solutions of this chemical in water, DMSO, 95% ethanol or acetone should be stable for 24 hours under normal lab conditions [RAD].

*OTHER PHYSICAL DATA:
Odorless; bitter taste
Saturated solution is neutral or slightly acid to litmus
Dissociation constant: pKa 8.3 @ 20 C
Maximum chloroform/water coefficient: 0.92 @ pH 6.0

-TOXICITY
========

*NIOSH REGISTRY NUMBER: YR1400000

*TOXICITY: **(abbreviations)**

typ. dose	mode	specie	amount	units	other
LDLo	ipr	rat	400	mg/kg	
LD50	orl	rat	1980	mg/kg	
TDLo	orl	chd	165	mg/kg/2W-I	
TDLo	orl	man	116	mg/kg/11W-I	
TDLo	orl	wmn	900	mg/kg/21W-I	
LDLo	orl	wmn	84	mg/kg/2W-I	
LDLo	unr	mus	750	ug/kg	
LDLo	unr	rat	750	ug/kg	

*AQTX/TLM96: Not available

*SAX TOXICITY EVALUATION:
THR: An experimental carcinogen, teratogen, equivocal tumorigenic agent and neoplastigen.

*CARCINOGENICITY:
Tumorigenic Data:
TDLo: orl-gpg 37 gm/kg/2Y-C
TDLo: orl-ham 653 gm/kg/70W-C
TDLo: orl-mus 600 gm/kg/73W-C

Review: IARC Cancer Review: Animal Sufficient Evidence
IARC Cancer Review: Human Inadequate Evidence
IARC possible human carcinogen (Group 2B) [610]
Status: EPA Carcinogen Assessment Group [610]
NTP anticipated human carcinogen [610]
NTP Fourth Annual Report on Carcinogens, 1984

*MUTATION DATA:

test	lowest dose	test	lowest dose
dni-hmn:lym	100 mg/L	mmo-smc	1 gm/L

*TERATOGENICITY:
Reproductive Effects Data:
TDLo: orl-gpg 1470 mg/kg (38-58D preg)
TDLo: orl-rat 4600 mg/kg (70D pre/1-22D preg)
TDLo: orl-rat 400 mg/kg (20-21D preg)
TDLo: orl-rat 1100 mg/kg (1-22D preg)
TDLo: orl-rat 500 mg/kg (18-22D preg/20D post)
TDLo: orl-rat 1050 mg/kg (21D post)
TDLo: orl-rbt 330 mg/kg (11-25D preg)
TDLo: orl-wmn 1818 mg/kg (33D pre/1-39W preg)
TDLo: orl-wmn 1620 mg/kg (1-39W preg)
TDLo: par-mam 615 ug/kg (29-32D preg)

*STANDARDS, REGULATIONS & RECOMMENDATIONS:
Standards and Regulations: OSHA Standard-air: Not regulated
ACGIH: None
NIOSH Criteria Document: None
NFPA Hazard Rating: Health (H): None
Flammability (F): None
Reactivity (R): None

*OTHER TOXICITY DATA:
Review: Toxicology Review-2
Status: EPA TSCA Chemical Inventory, 1986
EPA Genetox Program 1986, Positive: Carcinogenicity-mouse/rat
Meets criteria for proposed OSHA Medical Records Rule

-OTHER DATA (Regulatory)
==========

*PROPER SHIPPING NAME (IATA): Not restricted

*UN/ID NUMBER:

*HAZARD CLASS: SUBSIDIARY RISK: PACKING GROUP:

*LABELS REQUIRED:

*PACKAGING: PASSENGER: PKG. INSTR.: MAXIMUM QUANTITY:
CARGO : PKG. INSTR.: MAXIMUM QUANTITY:

*SPECIAL PROVISIONS:

*USES:
Anti-thyroid agent for hyperthyroidism; in veterinary medicine for antithyroid activity and to promote fattening; may have a possible use in the treatment of alcoholic hepatitis.

*COMMENTS:
Small amounts of thiourea may be present as an impurity.

-HANDLING PROCEDURES
==========

*ACUTE/CHRONIC HAZARDS:
There is sufficient evidence that this compound is carcinogenic in animals [015,395]. It is harmful if swallowed, inhaled or absorbed through the skin. It may cause irritation [269]. When heated to decomposition, this compound emits very toxic fumes of SOx and NOx [042,269]. It may also emit toxic fumes of CO and CO2 [269].

*MINIMUM PROTECTIVE CLOTHING: Not available

*RECOMMENDED GLOVE MATERIALS:
Recommended Glove Type For Use With Neat (Undiluted) Chemical:
Recommendations based on permeation test results are made for handling the neat (undiluted) chemical. If this chemical makes direct contact with your glove, or if a tear, puncture or hole develops, replace them at once.

Suggested Glove Type(s) (RAD): No information available

*RECOMMENDED RESPIRATOR:
Where the neat test chemical is weighed and diluted, wear a NIOSH-approved half face respirator equipped with a combination filter cartridge, i.e. organic vapor/acid gas/HEPA (specific for organic vapors, HCl, acid gas, SO2 and a high efficiency particulate filter).

*OTHER:
Since this chemical is a known or suspected carcinogen you should contact a physician for advice regarding the possible long term health effects and potential recommendation for medical monitoring. Recommendations from the physician will depend upon the specific compound, its chemical, physical and

toxicity properties, the exposure level, length of exposure, and the route of exposure.

*STORAGE PRECAUTIONS:
You should protect this chemical from exposure to light. Keep the container tightly closed under an inert atmosphere, and store under refrigerated temperatures.

*SPILLS AND LEAKAGE:
If you spill this chemical, dampen the solid spill material with 5% ammonium hydroxide, then transfer the dampened material to a suitable container. Use absorbent paper dampened with 5% ammonium hydroxide to pick up any remaining material. Your contaminated clothing and the absorbent paper should be sealed in a vapor-tight plastic bag for eventual disposal. Wash all contaminated surfaces with 5% ammonium hydroxide followed by washing with a soap and water solution. Do not reenter the contaminated area until the Safety Officer (or other responsible person) has verified that the area has been properly cleaned.

*DISPOSAL AND WASTE TREATMENT: Not available

-EMERGENCY PROCEDURES
==========

*SKIN CONTACT:
IMMEDIATELY flood affected skin with water while removing and isolating all contaminated clothing. Gently wash all affected skin areas thoroughly with soap and water.
If symptoms such as redness or irritation develop, IMMEDIATELY call a physician and be prepared to transport the victim to a hospital for treatment.

*INHALATION:
IMMEDIATELY leave the contaminated area; take deep breaths of fresh air. IMMEDIATELY call a physician and be prepared to transport the victim to a hospital even if no symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop.
Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Respirator Recommendation.

*EYE CONTACT:
First check the victim for contact lenses and remove if present. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
Do not put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.

IMMEDIATELY transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

*INGESTION:
DO NOT INDUCE VOMITING. If the victim is conscious and not convulsing, give 1 or 2 glasses of water to dilute the chemical and IMMEDIATELY call a hospital or poison control center. Be prepared to transport the victim to a hospital if advised by a physician.
If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body. DO NOT INDUCE VOMITING. IMMEDIATELY transport the victim to a hospital.

*SYMPTOMS:
Symptoms of exposure to this compound include recurrent painful skin lesions, fatigue, migratory polyanthralgias of hands and knees, palpable spleen, splenomegaly, amenorrhea, low-grade fever, gingivostomatitis, weakness, weight loss, dark red-brown colored urine, necrotizing vasculitis, leukopenia, cutaneous vasculitis, nasal congestion, enlarged thyroid, necrotic ulcerations on the lower extremities, bloody nasal discharge and cough [051,072]. Other symptoms include fever, sore throat, rash and malaise [051,072,301]. The most serious reaction to this chemical may be agranulocytosis [295,301,406]. It may also cause pain and stiffness in the joints, paresthesias, headache, nausea and loss or depigmentation of hair. On rare occasions, exposure to this material may cause drug fever, hepatitis and nephritis [406]. Other symptoms include urticaria, anorexia, hypoprothrombinemia with purpura and hepatic injury [301]. Exposure may also cause a tendency to hemorrhage, lupus-like syndrome, hypothyroidism, galactorrhea, migratory polyarthritis, reversible tinnitus, hearing loss, hypocalcemia, jaundice, hepatic necrosis and liver disease similar to chronic active hepatitis. It may also cause goiter in infants born to women following exposure to this compound [295].

-SOURCES
=======

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Return to NTP Home Page

NTP welcomes your e-mail comments and suggestions.
Please send them to: **NTP Webmaster (ntpwm@niehs.nih.g**
Last revised: 25 July 2001

-=-

iem Service, Inc. PS-1049
ATERIAL SAFETY DATA SHEET

voice: CS214030 PO: P293087

inted: 01/22/2001
st Revised: November 6, 1992

CTION 1 - CHEMICAL PRODUCT and COMPANY IDENTIFICATION

talog Number: PS-1049
scription: Vinclozolin
her Name(s): 3-(3.5-Dichlorophenyl)-5-ethenyl-5-methyl-2.4-oxazolidinedio

pplied by CHEM SERVICE, Inc. PO BOX 599, WEST CHESTER, PA 19381 (610)-692-3026
ERGENCY PHONE: 1-610-692-3026

CTION 2 - COMPOSITION, INFORMATION ON INGREDIENTS

S No.: 50471-44-8
scription: Vinclozolin
NECS No.: Not Available
zard Symbols: Not Available

CTION 3 - HAZARDS IDENTIFICATION

ntact lenses should not be worn in the laboratory.
l chemicals should be considered hazardous - Avoid direct physical contact!
n cause eye irritation. Can cause skin irritation.
y be harmful if absorbed through the skin. May be harmful if inhaled.
y be harmful if swallowed.

CTION 4 - FIRST AID MEASURES

antidote is a substance intended to counteract the effect of a poison. It should be
ministered only by a physician or trained emergency personnel. Medical advice can be
tained from a POISON CONTROL CENTER.

case of contact: Flush eyes continuously with water for 15-20 minutes. Flush skin with water
r 15-20 minutes. If no burns have occurred-use soap and water to cleanse skin.
inhaled remove patient to fresh air. Administer oxygen if patient is having difficulty
eathing. If patient has stopped breathing administer artificial respirations.
patient is in cardiac arrest administer CPR.
ntinue life supporting measures until medical assistance has arrived.

CTION 5 - FIRE AND EXPLOSION DATA

ash Point: Not Available
tinguishing Media:
Carbon dioxide, dry chemical powder or spray.
per Explosion Limit: Not Available
wer Explosion Limit: Not Available
toignition Temperature: Not Available
PA Hazard Rating: Not Available

at No.: PS-1049
age: 2

ECTION 6 - ACCIDENTAL RELEASE MEASURES

pills or leaks: Evacuate area. Wear appropriate OSHA regulated equipment. Ventilate area.
weep up and place in an appropriate container. Hold for disposal.
ash contaminated surfaces to remove any residues.
emove contaminated cloting and wash befire reuse.

ECTION 7 - HANDLING AND STORAGE

ndling:
is chemical should be handled only in a hood. Eye shields should be worn.
se appropriate OSHA/MSHA approved safety equipment.
oid contact with skin, eyes and clothing. Avoid ingestion and inhalation
sh thoroughly after handling.

orage:
tore in a cool dry place. Store only with compatible chemicals.
ep tightly closed.

ECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

HA PEL (TWA): Not Available
GIH TLV (TWA): Not Available
GIH TLV (STEL): Not Available

rsonal Protective Equipment
Eyes: Wear Safety Glasses.
Skin: Wear appropriate protective gloves to prevent skin exposure.
Clothing: Wear appropriate protective clothing to minimize contact with skin.
spirators: A respiratory protection program that meets OSHA's 29 CFR 1910.134 requirements must be followed whenever workplace conditions warrant a respirator's use.

ECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

lor:	Colorless
ase:	Crystalline solid
lting Point:	108 C
iling Point:	Not Available
ecific Gravity:	Not Available
por Pressure:	Not Available
por Density:	Not Available
lubility in Water:	Very slightly soluble
or:	Not Available
aporation Rate (Butyl acetate=1):	Not Available
lecular Weight	286.12
lecular Formula	C12H9Cl2NO3

ECTION 10 - STABILITY AND REACTIVITY

acts with Acid halides and anhydrides. Decomposes under alkaline conditions.

ECTION 11 - TOXICOLOGY INFORMATION

TECS: Not Available
-al Rat or Mouse LD50: 10000mg/kg
ermal Rat or Mouse LD50: N/A
it or Mouse LC50: Not Available

arcinogenicity
OSHA: No
IARC: No
NTP: No
ACGIH: No
NIOSH: No
Other: No

ECTION 12 - ECOLOGICAL INFORMATION

cotoxicity: Not Available
vironmental Fate: Not Available

ECTION 13 - DISPOSAL CONSIDERATIONS

ISPOSAL: Burn in a chemicals incinerator equipped with an afterburner and scrubber.

ECTION 14 - TRANSPORTATION INFORMATION

t regulated as a hazardous material.

ECTION 15 - REGULATORY INFORMATION

ropean Labeling in Accordance with EC Directives
zard Symbols: Not Available
sk Phrases
Not Available
afety Phrases
Not Available

ECTION 16 - OTHER INFORMATION

e above information is believed to be correct on the date it is published and must not be onsidered all inclusive. The information has been obtained only by a search of available terature and is only a guide for handling the chemicals. OSHA regulations require that other hazards become evident, an upgraded MSDS must be made avalible to the employee thin three months. RESPONSIBILITY for updates lies with the employer and not with IEM SERVICE, Inc.

rsons not specifically and properly trained should not handle this chemical or s container. This MSDS is provided without any warranty expressed or implied, cluding merchantability or fitness for any particular purpose.

at No.: PS-1049
age: 4

his product is furnished FOR LABORATORY USE ONLY! Our products may NOT BE USED as drugs, osmetics, agricultural or pesticidal products, food additives or as household chemicals.

PS-372

iem Service, Inc.
ATERIAL SAFETY DATA SHEET

voice: CS222794 PO: 11067493EDSF

inted: 10/29/2001
st Revised: July 6, 2001

CTION 1 - CHEMICAL PRODUCT and COMPANY IDENTIFICATION

talog Number: PS-372
scription: Linuron
her Name(s): 3-[3,4-Dichlorophenyl]-1-methoxy-1-methylurea

pplied by CHEM SERVICE, Inc. PO BOX 599, WEST CHESTER, PA 19381 (610)-692-3026
ERGENCY PHONE: 1-610-692-3026

CTION 2 - COMPOSITION, INFORMATION ON INGREDIENTS

S No.: 330-55-2
scription: Linuron
NECS No.: 206-356-5
ard Symbols: Xn

CTION 3 - HAZARDS IDENTIFICATION

ntact lenses should not be worn in the laboratory.
l chemicals should be considered hazardous - Avoid direct physical contact!
n cause eye irritation. Can cause skin irritation.
st and/or vapors can cause irritation to respiratory tract.
be irritating to mucous membranes. May be harmful if absorbed through the skin.
be harmful if inhaled. May be harmful if swallowed.

CTION 4 - FIRST AID MEASURES

antidote is a substance intended to counteract the effect of a poison. It should be
ministered only by a physician or trained emergency personnel. Medical advice can be
ained from a POISON CONTROL CENTER.

case of contact: Flush eyes continuously with water for 15-20 minutes. Flush skin with water
r 15-20 minutes. If no burns have occurred-use soap and water to cleanse skin.
inhaled remove patient to fresh air. Administer oxygen if patient is having difficulty
eathing. If patient has stopped breathing administer artificial respirations.
patient is in cardiac arrest administer CPR.
ntinue life supporting measures until medical assistance has arrived.
move and wash contaminated clothing.
patient is exhibiting signs of shock - Keep warm and quiet.
ntact Poison Control Center immediately if necessary. Induce vomiting if swallowed.
not administer liquids or induce vomiting to an unconscious or convulsing person.
patient is vomiting-watch closely to make sure airway does not become obstructed by vomit.
medical attention if necessary.

CTION 5 - FIRE AND EXPLOSION DATA

sh Point: Not Available

ECTION 5 - FIRE AND EXPLOSION DATA CONTINUED

tinguishing Media:
Carbon dioxide, dry chemical powder or spray.
pper Explosion Limit: Not Available
wer Explosion Limit: Not Available
utoignition Temperature: Not Available
FPA Hazard Rating: Not Available

ECTION 6 - ACCIDENTAL RELEASE MEASURES

ills or leaks: Evacuate area. Wear appropriate OSHA regulated equipment. Ventilate area.
eep up and place in an appropriate container. Hold for disposal.
ash contaminated surfaces to remove any residues.
emove contaminated cloting and wash befire reuse.

ECTION 7 - HANDLING AND STORAGE

ndling:
is chemical should be handled only in a hood. Eye shields should be worn.
e appropriate OSHA/MSHA approved safety equipment.
oid contact with skin, eyes and clothing. Avoid ingestion and inhalation
sh thoroughly after handling.

orage:
ore in a cool dry place. Store only with compatible chemicals.
ep tightly closed.

CTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

HA PEL (TWA): Not Available
GIH TLV (TWA): Not Available
GIH TLV (STEL): Not Available

rsonal Protective Equipment
Eyes: Wear Safety Glasses.
Skin: Wear appropriate protective gloves to prevent skin exposure.
Clothing: Wear appropriate protective clothing to minimize contact with skin.
espirators: A respiratory protection program that meets OSHA's 29 CFR 1910.134 requirements must be followed whenever workplace conditions warrant a respirator's use.

CTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

lor: Colorless
se: Crystalline solid
lting Point: 93-94 C
iling Point: Not Available
ecific Gravity: Not Available
por Pressure: Not Available
por Density: Not Available

No.: PS-372
ge: 3

lubility in Water:	Not Available
lor:	Not Available
aporation Rate (Butyl acetate=1):	Not Available
olecular Weight	249.11
olecular Formula	C9H10Cl2N2O2

ECTION 10 - STABILITY AND REACTIVITY

nsitive to light - dark color does not affect purity. Sensitive to heat.
composes under alkaline conditions. Decomposes under acidic conditions.

CTION 11 - TOXICOLOGY INFORMATION

TECS: YS9100000
al Rat or Mouse LD50: 4000mg/kg
rmal Rat or Mouse LD50: >2500
or Mouse LC50: Not Available

rcinogenicity
OSHA: No
IARC: No
NTP: No
ACGIH: No
NIOSH: No
Other: No

CTION 12 - ECOLOGICAL INFORMATION

toxicity: Not Available
vironmental Fate: Not Available

CTION 13 - DISPOSAL CONSIDERATIONS

SPOSAL: Burn in a chemicals incinerator equipped with an afterburner and scrubber.

CTION 14 - TRANSPORTATION INFORMATION

t regulated as a hazardous material.

CTION 15 - REGULATORY INFORMATION

ropean Labeling in Accordance with EC Directives
ard Symbols: Xn
sk Phrases
R40
Possible risk of irreversible effects.

fety Phrases
S36/37
Wear suitable protective clothing and gloves.

ECTION 16 - OTHER INFORMATION

e above information is believed to be correct on the date it is published and must not be nsidered all inclusive. The information has been obtained only by a search of available terature and is only a guide for handling the chemicals. OSHA regulations require that other hazards become evident, an upgraded MSDS must be made avalible to the employee thin three months. RESPONSIBILITY for updates lies with the employer and not with EM SERVICE, Inc.

rsons not specifically and properly trained should not handle this chemical or s container. This MSDS is provided without any warranty expressed or implied, cluding merchantability or fitness for any particular purpose.

is product is furnished FOR LABORATORY USE ONLY! Our products may NOT BE USED as drugs, smetics, agricultural or pesticidal products, food additives or as household chemicals.

Enter a chemical name, CAS Number, molecular formula, or molecular weight

New Search

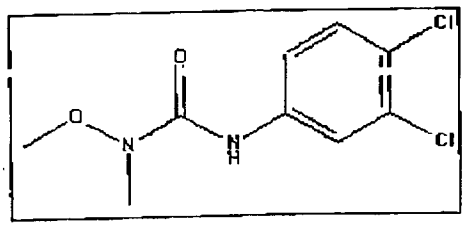
Or choose: Substructure Query with Plug-In or Structure Query with Java

Linuron [330-55-2]

Synonyms: Lorox; N'-(3,4-Dichlorophenyl)-N-methoxy-N-methylurea; methoxydiuron; du Pont Herbicide 3
Linex; Alafon; Lorox Plus; Linex 4L; Lorox 4L; Lorox 50W; Lorox DF; Lorox L; Linorox; Sarclex; Aflon; I
1-Methoxy-1-methyl-3-(3,4-dichlorophenyl)urea; 3-(3,4-Dichlorophenyl)-1-methoxy(methyl)urea; Cephalon
Methoxy-1-methyl-3-(3,4-dichlorophenyl)urea; Premalin; Urea, 1-(3,4-dichlorophenyl)-3-methoxy-3-methyl-
3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea; N-(3,4-Dichlorophenyl)-N'-methoxy-N'-methylurea; Linur

$C_9H_{10}Cl_2N_2O_2$

249.0962



View with ChemDraw Plugin
Save in CDX format

Add Compound Add or Change Property Add Link Feedback

Eye Protection: EYE SHIELDS
Work Hygienic Practices: REMOVE/LAUNDER CONTAMINATED CLOTHING BEFORE REUSE. CONTACT LENSES SHOULDN'T BE WORN IN THE LABORATORY.
Suppl. Safety & Health Data: PERSONS NOT SPECIFICALLY/PROPERLY TRAINED SHOULDN'T HANDLE THIS CHEMICAL/ITS CONTAINER. ALL CHEMICALS SHOULD BE CONSIDERED HAZARDOUS-AVOID DIRECT PHYSICAL CONTACT. DATA INFORMATION IS FOR ACETONE.

==========

Transportation Data

==========

==========

Disposal Data

==========

==========

Label Data

==========

Extinguishing Media: CO2, DRY CHEMICAL POWDER/SPRAY

Reactivity Data

Stability: YES
Materials To Avoid: STRONG OXIDIZING AGENTS
Hazardous Poly Occur: NO

Health Hazard Data

LD50-LC50 Mixture: ORAL LD50(RAT): 6000 MG/KG
Route Of Entry - Inhalation: YES
Route Of Entry - Skin: YES
Route Of Entry - Ingestion: YES
Health Haz Acute And Chronic: SKIN/EYES: CAN CAUSE IRRITATION. CAN BE IRRITATING TO MUCOUS MEMBRANES. MAY BE HARMFUL IF ABSORBED THROUGH THE SKIN, INHALED/IF SWALLOWED. EXPOSURE CAN CAUSE KIDNEY/LIVER DAMAGE.
Carcinogenicity - NTP: NO
Carcinogenicity - IARC: NO
Carcinogenicity - OSHA: NO
Explanation Carcinogenicity: NONE
Signs/Symptoms Of Overexp: IRRITATION
IF NO BURNS HAVE OCCURRED, CLEANSE W/SOAP & WATER. INHALATION: REMOVE TO FRESH AIR. GIVE OXYGEN/CPR IF NEEDED. IF IN SHOCK, KEEP WARM/QUIET. INGESTION: INDUCE VOMITING. DON'T GIVE LIQUIDS/INDUCE VOMITING IF UNCONSCIOUS/CONVULSING. IF VOMITING, WATCH CLOSELY TO MAKE SURE AIRWAY DOESN'T BECOME OBSTRUCTED BY VOMIT. OBTAIN MEDICAL ATTENTION IN ALL CASES.

Precautions for Safe Handling and Use

Steps If Matl Released/Spill: EVACUATE AREA. WEAR OSHA REGULATED EQUIPMENT. VENTILATE AREA. SWEEP UP & PLACE IN AN APPROPRIATE CONTAINER. HOLD FOR DISPOSAL. WASH CONTAMINATED SURFACES TO REMOVE ANY RESIDUES.
Waste Disposal Method: BURN IN A CHEMICALS INCINERATOR EQUIPPED W/AN AFTERBURNER & SCRUBBER/DISPOSE OF IN ACCORDANCE W/LOCAL, STATE & FEDERAL REGULATIONS.
Precautions-Handling/Storing: KEEP TIGHTLY CLOSED. STORE IN A COOL, DRY PLACE. STORE ONLY W/COMPATIBLE CHEMICALS. THIS PRODUCT IS FURNISHED FOR LABORATORY USE ONLY.
Other Precautions: AVOID CONTACT W/SKIN, EYES & CLOTHING. DON'T BREATHE VAPORS. PRODUCT MAY NOT BE USED AS DRUGS, COSMETICS, AGRICULTURAL/ PESTICIDAL PRODUCTS, FOOD ADDITIVES/AS HOUSEHOLD CHEMICALS.

Control Measures

Respiratory Protection: USE APPROPRIATE OSHA/MSHA APPROVED SAFETY EQUIPMENT.
Ventilation: THIS CHEMICAL SHOULD BE HANDLED ONLY IN A HOOD.

CHEM SERVICE -- F910 METHOXYCHLOR
MATERIAL SAFETY DATA SHEET
NSN: 655000F051063
Manufacturer's CAGE: 8Y898
Part No. Indicator: A
Part Number/Trade Name: F910 METHOXYCHLOR

==========

General Information

==========

Company's Name: CHEM SERVICE INC
Company's Street: 660 TOWER LN
Company's P. O. Box: 3108
Company's City: WEST CHESTER
Company's State: PA
Company's Country: US
Company's Zip Code: 19381-3108
Company's Emerg Ph #: 215-386-2100/215-692-3026
Company's Info Ph #: 215-692-3026/800-452-9994
Record No. For Safety Entry: 001
Tot Safety Entries This Stk#: 001
Status: SE
Date MSDS Prepared: 25JAN95
Safety Data Review Date: 19SEP96
Preparer's Company: CHEM SERVICE INC
Preparer's St Or P. O. Box: 660 TOWER LN
Preparer's City: WEST CHESTER
Preparer's State: PA
Preparer's Zip Code: 19381-3108
MSDS Serial Number: CCDMW

==========

Ingredients/Identity Information

==========

Proprietary: NO
Ingredient: METHOXYCHLOR (IARC CARCINOGEN - GROUP 3) *96-3*
Ingredient Sequence Number: 01
NIOSH (RTECS) Number: KJ3675000
CAS Number: 72-43-5
OSHA PEL: 15 MG/CUM
ACGIH TLV: 10 MG/CUM

==========

Physical/Chemical Characteristics

==========

Appearance And Odor: COLORLESS CRYSTALLINE SOLID W/FRUITY/PLEASANT ODOR
Melting Point: 186.8-192F
Solubility In Water: INSOLUBLE

==========

Fire and Explosion Hazard Data

==========

Section 16. Other Information

MSDS Code	K3096
References	Not available.
Other Special Considerations	Not available.

Validated by C. A. Binas on 2/17/2000.	Verified by C. A. Binas. Printed 11/16/2001.

CALL (310) 516-8000

Notice to Reader

All chemicals may pose unknown hazards and should be used with caution. This Material Safety Data Sheet (MSDS) applies only to the material as packaged. If this product is combined with other materials, deteriorates, or becomes contaminated, it may pose hazards not mentioned in this MSDS. It shall be the user's responsibility to develop proper methods of handling and personal protection based on the actual conditions of use. While this MSDS is based on technical data judged to be reliable, Spectrum Quality Products, Inc. assumes no responsibility for the completeness or accuracy of the information contained herein.

Ketoconazole

Section 15. Other Regulatory Information and Pictograms

Federal and State Regulations: No products were found.

California Proposition 65 Warnings

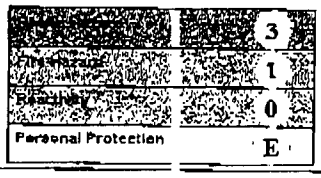
Other Regulations: OSHA: Hazardous by definition of Hazard Communication Standard (29 CFR 1910.1200).

Other Classifications

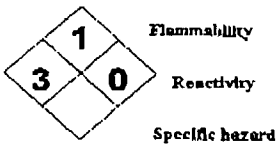
WHMIS (Canada): Class D-1B: Material causing immediate and serious toxic effects (TOXIC).

DSCL (EEC):
R25- Toxic if swallowed.
R40- Possible risks of irreversible effects.
62- Possible risk of impaired fertility.

HMIS (U.S.A.)



National Fire Protection Association (U.S.A.)



WHMIS (Canada) (Pictograms)

DSCL (Europe) (Pictograms)

TDG (Canada) (Pictograms)

ADR (Europe) (Pictograms)

Protective Equipment

Gloves.

Lab coat.

Dust respirator. Be sure to use an approved/certified respirator or equivalent. Wear appropriate respirator when ventilation is inadequate.

Safety glasses.

Continued on Next Page

Section 11. Toxicological Information

Routes of Entry	Absorbed through skin. Eye contact. Ingestion.
Toxicity to Animals	Acute oral toxicity (LD50): 166 mg/kg [Rat].
Chronic Effects on Humans	DEVELOPMENTAL TOXICITY: Classified Reproductive system/toxin/female, Reproductive system/toxin/male [POSSIBLE]. Classified Development toxin [NONE]. The substance is toxic to liver, endocrine.
Other Toxic Effects on Humans	Slightly hazardous in case of skin contact (irritant).
Special Remarks on Toxicity to Animals	Not available.
Special Remarks on Chronic Effects on Humans	Not available.
Special Remarks on other Toxic Effects on Humans	Not available.

Section 12. Ecological Information

Ecotoxicity	Not available.
BOD5 and COD	Not available.
Products of Biodegradation	Possibly hazardous short term degradation products are not likely. However, long term degradation products may arise.
Toxicity of the Products of Biodegradation	The products of degradation are less toxic than the product itself.
Special Remarks on the Products of Biodegradation	Not available.

Section 13. Disposal Considerations

Waste Disposal

Section 14. Transport Information

DOT Classification	Class 6.1: Poisonous material.
Identification	Shipping name: Toxic Solid, Organic, n.o.s. (Ketoconazole) UNNA: UN2811 PG: III
Special Provisions for Transport	Not available.
DOT (Pictograms)	

Continued on Next Page

Section 8. Exposure Controls/Personal Protection

Engineering Controls	Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. If user operations generate dust, fume or mist, use ventilation to keep exposure to airborne contaminants below the exposure limit.
Personal Protection	Safety glasses. Lab coat. Dust respirator. Be sure to use an approved/certified respirator or equivalent. Gloves.
Personal Protection in Case of a Large Spill	Splash goggles. Full suit. Dust respirator. Boots. Gloves. A self contained breathing apparatus should be used to avoid inhalation of the product. Suggested protective clothing might not be sufficient; consult a specialist BEFORE handling this product.
Exposure Limits	Not available.

Section 9. Physical and Chemical Properties

Physical state and appearance	Solid.
Molecular Weight	531.48 g/mole
pH (1% soln/water)	Not available.
Boiling Point	Not available.
Melting Point	Not available.
Critical Temperature	Not available.
Specific Gravity	Not available.
Vapor Pressure	Not applicable.
Vapor Density	Not available.
Volatility	Not available.
Odor Threshold	Not available.
Water/Oil Dist. Coeff.	Not available.
Ionicity (in Water)	Not available.
Dispersion Properties	Not available.
Solubility	Not available.

Odor	Not available.
Taste	Not available.
Color	White Crystal Powder

Section 10. Stability and Reactivity Data

Stability	The product is stable.
Instability Temperature	Not available.
Conditions of Instability	Not available.
Incompatibility with various substances	Not available.
Corrosivity	Non-corrosive in presence of glass.
Special Remarks on Reactivity	Not available.
Special Remarks on Corrosivity	Not available.
Polymerization	No.

Continued on Next Page

Section 4. First Aid Measures

Eye Contact	NO known EFFECT on eye contact, rinse with water for a few minutes.
Skin Contact	After contact with skin, wash immediately with plenty of water. Gently and thoroughly wash the contaminated skin with running water and non-abrasive soap. Be particularly careful to clean folds, crevices, creases and groin. Cover the irritated skin with an emollient. If irritation persists, seek medical attention. Wash contaminated clothing before reusing.
Serious Skin Contact	Not available.
Inhalation	Allow the victim to rest in a well ventilated area. Seek immediate medical attention.
Serious Inhalation	Evacuate the victim to a safe area as soon as possible. Loosen tight clothing such as a collar, tie, belt or waistband. If breathing is difficult, administer oxygen. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek medical attention.
Ingestion	Do not induce vomiting. Loosen tight clothing such as a collar, tie, belt or waistband. If the victim is not breathing, perform mouth-to-mouth resuscitation. Seek immediate medical attention.
Serious Ingestion	Not available.

Section 5. Fire and Explosion Data

Flammability of the Product	May be combustible at high temperature.
Auto-Ignition Temperature	Not available.
Flash Points	Not available.
Flammable Limits	Not available.
Products of Combustion	These products are carbon oxides (CO, CO2), nitrogen oxides (NO, NO2...).
Fire Hazards in Presence of Various Substances	Slightly flammable to flammable in presence of open flames and sparks.
Explosion Hazards in Presence of Various Substances	Risks of explosion of the product in presence of mechanical impact: Not available. Risks of explosion of the product in presence of static discharge: Not available.
Fire Fighting Media and Instructions	SMALL FIRE: Use DRY chemical powder. LARGE FIRE: Use water spray, fog or foam. Do not use water jet.
Special Remarks on Fire Hazards	Not available.
Special Remarks on Explosion Hazards	Not available.

Section 6. Accidental Release Measures

Small Spill	Use appropriate tools to put the spilled solid in a convenient waste disposal container.
Large Spill	Use a shovel to put the material into a convenient waste disposal container.

Section 7. Handling and Storage

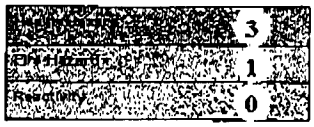
Precautions	Keep locked up Keep away from heat Keep away from sources of ignition. Empty containers pose a fire risk, evaporate the residue under a fume hood. Ground all equipment containing material. Do not ingest. Do not breathe dust Wear suitable protective clothing If ingested, seek medical advice immediately and show the container or the label.
Storage	Keep container dry. Keep in a cool place. Ground all equipment containing material. Keep container tightly closed. Keep in a cool, well-ventilated place. Highly toxic or infectious materials should be stored in a separate locked safety storage cabinet or room.

Continued on Next Page

SPECTRUM

GARDENA, CA
NEW BRUNSWICK, NJ

Material Safety Data Sheet

NFPA	HMIS	Personal Protective Equipment
		
		See Section 15.

Section 1. Chemical Product and Company Identification

Common Name/ Trade Name	**Ketoconazole**	Catalog Number(s).	K1149
		CAS#	65277-42-1
Manufacturer	SPECTRUM QUALITY PRODUCTS, INC. 14422 S. SAN PEDRO STREET GARDENA, CA 90248	RTECS	TK7912300
		TSCA	TSCA inventory: No products were found.
Commercial Name(s)	Not available.	CI#	Not available.
Synonym	Piperazine, 1-acetyl-4-(4-((2-(2,4-dichlorophenyl)-2-(1H-Imidazol-1-ylmethyl)-1,3-	**IN CASE OF EMERGENCY** **CHEMTREC (24hr) 800-424-9300**	
Chemical Name	Ketoconazole	CALL (310) 516-8000	
Chemical Family	Not available.		
Chemical Formula	C26-H28-CL2-N4-O4		
Supplier	SPECTRUM QUALITY PRODUCTS, INC. 14422 S. SAN PEDRO STREET GARDENA, CA 90248		

Section 2. Composition and Information on Ingredients

		Exposure Limits			
Name	CAS #	TWA (mg/m³)	STEL (mg/m³)	CEIL (mg/m³)	% by Weight
1) Ketoconazole					100

Toxicological Data on Ingredients	Ketoconazole: ORAL (LD50):	Acute: 166 mg/kg [Rat]. 618 mg/kg [Mouse]. 178 mg/kg [Guinea pig].

Section 3. Hazards Identification

Potential Acute Health Effects	Slightly hazardous in case of skin contact (irritant), of eye contact (irritant). Severe over-exposure can result in death.
Potential Chronic Health Effects	**CARCINOGENIC EFFECTS:** Not available. **MUTAGENIC EFFECTS:** Not available. **TERATOGENIC EFFECTS:** Not available. **DEVELOPMENTAL TOXICITY:** Classified Reproductive system/toxin/female, Reproductive system/toxin/male [POSSIBLE]. Classified Development toxin [NONE]. The substance is toxic to liver, endocrine.

Continued on Next Page

NAUSEA, CENTRAL NERVOUS SYSTEM DEPRESSION, LOW BLOOD PRESSURE & RESPIRATORY FAILURE. PROLONGED CONTACT MAY CAUSE DERMATITIS. CHRONIC:NONE LISTED BY MANUFACTURER.
Protect Eye: Y
Protect Skin: Y
Protect Respiratory: Y
Label Name: ANALYTICAL PRODUCTS GROUP INC
Label Street: 2730 WASHINGTON BLVD
Label City: BELPRE
Label State: OH
Label Zip Code: 45714
Label Country: US
Label Emergency Number: 800-272-4442

LATER DISPOSAL. SAMPLE SOLUTIONS SHOULD BE ABSORBED W/CHARCOAL OR OTHER ORGANIC ABSORBANT & INCINERATED. FLUSH AREA W/WATER.
Neutralizing Agent: NONE SPECIFIED BY MANUFACTURER.
Waste Disposal Method: DISPOSE OF I/A/W ALL APPLICABLE FEDERAL, STATE & LOCAL REGULATIONS.
Precautions-Handling/Storing: KEEP CONTAINER TIGHTLY CLOSED. STORE IN A COOL, DRY, WELL-VENTILATED, FLAMMABLE LIQUID STORAGE AREA. ISOLATE FROM INCOMPATIBLE MATERIALS.
Other Precautions: DO NOT HEAT OR EVAPORATE ANALYTICAL STANDARDS TO DRYNESS. SHUT OFF IGNITION SOURCES; NO FLARES, SMOKING OR FLAMES IN AREA.

Control Measures

Respiratory Protection: RESP PROT REQD IF AIRBORNE CONC EXCEEDS PEL (750 PPM). AT CONCS UP TO 5000 PPM NIOSH/MSHA APPRVD CHEM CARTRIDGE RESP W/ORG VAP CARTRIDGE IS REC. ABOVE THIS LEVEL, NIOSH/MSHA APPRVD SCBA IS REC. (20,000 PPM IS IMMED DANGEROUS TO LIFE/HLTH).
Ventilation: LOCAL EXHAUST.
Protective Gloves: BUTYL, NEOPRENE OR LATEX RUBBER GLOVES.
Eye Protection: ANSI APVD CHEMICAL SAFETY GOGGLES (FP N)
Other Protective Equipment: MAINT ANSI APVD EYE WASH FOUNTAIN & QUICK-DRENCH FACILS IN WORK AREA. GOOD CHEM HYGIENE PRACTICE REQS LAB COAT/APRON.
Work Hygienic Practices: NONE SPECIFIED BY MANUFACTURER.
Suppl. Safety & Health Data: EXPLO HAZ:MAY CAUSE FIRE. MATLS TO AVOID:& CHLORINE COMPOUNDS, STRONG ACIDS, ESP. SULFURIC, NITRIC, HYDROCHLORIC.

Transportation Data

Disposal Data

Label Data

Label Required: YES
Technical Review Date: 07OCT93
Label Date: 28SEP93
Label Status: G
Common Name: PESTICIDES QC STANDARD
Chronic Hazard: NO
Signal Word: DANGER!
Acute Health Hazard-Moderate: X
Contact Hazard-Slight: X
Fire Hazard-Severe: X
Reactivity Hazard-None: X
Special Hazard Precautions: EXTREMELY FLAMMABLE. ACUTE:FOR ACETONE:OSHA/ACGIH TWA IS 750 PPM, 20,000 PPM IS IMMEDIATELY DANGEROUS TO LIFE & HEALTH. IRRITATION OF SKIN, EYES, NOSE & THROAT. HEADACHE, DIZZINESS, VOMITING,

(WATER MAY BE INEFT). USE EXTINGUISHER MEDIA APPROP FOR SURROUND FIRE.
Special Fire Fighting Proc: USE NIOSH/MSHA APPROVED SCBA & FULL PROT EQUIP (FP N). MOVE CNTNRS FROM FIRE AREA IF IT CAN BE DONE W/OUT RISK. USE WATER TO KEEP FIRE-EXPOS CNTNRS COOL.
Unusual Fire And Expl Hazrds: VAP/AIR MIXTS ARE EXPLO. VAPS MAY FLOW ALONG SURFS TO DIST IGNIT SOURCES & FLASH BACK. CLSD CNTNRS EXPOS TO HEAT MAY EXPLODE. CONT W/STRONG OXIDIZERS (SUPDAT)

Reactivity Data

Stability: YES
Cond To Avoid (Stability): HEAT, FLAME, OTHER SOURCES OF IGNITION.
Materials To Avoid: ING 1:STRONG OXIDIZING AGENTS, STRONG BASES, HALOGEN ACIDS & HALOGEN CMPDS, CAUSTICS, AMINES & AMMONIA, CHLORINE(SUPDAT)
Hazardous Decomp Products: CARBON MONOXIDE, CARBON DIOXIDE, TOXIC FUMES OF CHLORINE.
Hazardous Poly Occur: NO
Conditions To Avoid (Poly): NOT RELEVANT

Health Hazard Data

LD50-LC50 Mixture: NONE SPECIFIED BY MANUFACTURER.
Route Of Entry - Inhalation: YES
Route Of Entry - Skin: YES
Route Of Entry - Ingestion: YES
Health Haz Acute And Chronic: FOR ACETONE:OSHA/ACGIH TWA IS 750 PPM, 20, 000 PPM IS IMMEDIATELY DANGEROUS TO LIFE & HEALTH. IRRITATION OF SKIN, EYES, NOSE & THROAT. HEADACHE, DIZZINESS, VOMITING, NAUSEA, CENTRAL NERVOUS SYSTEM DEPRESSION, LOW BLOOD PRESSURE & RESPIRATORY FAILURE. PROLONGED CONTACT MAY CAUSE DERMATITIS.
Carcinogenicity - NTP: NO
Carcinogenicity - IARC: NO
Carcinogenicity - OSHA: NO
Explanation Carcinogenicity: NOT RELEVANT
Signs/Symptoms of Overexp: SEE HEALTH HAZARDS.
Med Cond Aggravated By Exp: SKIN DISORDERS, EYE DISORDERS, CHRONIC RESPIRATORY DISEASE.
Emergency/First Aid Proc: SEE MED ASSISTANCE FOR TREATMENT, OBSERVATION & SUPPORT IF NECESSARY. EYE:FLUSH W/WATER FOR AT LST 15 MINS, SEEK MED ATTN. SKIN:WASH W/SOAP & WATER, USE PROTECTIVE CREAMS. INHAL: REMOVE TO FRESH AIR, IF NOT BREATHING, GIVE ARTF RESP. IF BREATHING IS DIFFICULT, GIVE OXYGEN, OBTAIN MED ASSISTANCE. INGEST:OBTAIN MED ASSISTANCE IF SWALLOWED. IF CONSCIOUS, GIVE LG AMTS OF WATER & INDUCE VOMITING.

Precautions for Safe Handling and Use

Steps If Matl Released/Spill: DILUTED STANDARD CAN BE ABSORBED W/SAND OR OTHER NON-COMBUSTIBLE ABSORBENT MATERIAL & PLACED INTO A CONTAINER FOR

Proprietary: NO
Ingredient: CYCLOHEXANE,1,2,3,4,5,6-HEXACHLORO-, ALPHA-ISOMER; (ALPHA-BHC) (BENZENE HEXACHLORIDE-ALPHA) (SARA III)
Ingredient Sequence Number: 18
Percent: <0.1
NIOSH (RTECS) Number: GV3500000
CAS Number: 319-84-6
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: CYCLOHEXANE,1,2,3,4,5,6-HEXACHLORO-,BETA-ISOMER; (BETA-BHC) (BENZENE HEXACHLORIDE-BETA) (SARA III)
Ingredient Sequence Number: 19
Percent: <0.1
NIOSH (RTECS) Number: GV4375000
CAS Number: 319-85-7
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: CYCLOHEXANE,1,2,3,4,5,6-HEXACHLORO-,DELTA-ISOMER; (DELTA-BHC) (BENZENE HEXACHLORIDE-DELTA) (SARA III)
Ingredient Sequence Number: 20
Percent: <0.1
NIOSH (RTECS) Number: GV4550000
CAS Number: 319-86-8
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

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Physical/Chemical Characteristics

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Appearance And Odor: ING 1: CLEAR, COLORLESS LIQUID; SWEET ODOR.
Boiling Point: SEE ING 1
Melting Point: SEE ING 1
Vapor Pressure (MM Hg/70 F): SEE ING 1
Vapor Density (Air=1): SEE ING 1
Specific Gravity: SEE ING 1
Evaporation Rate And Ref: ING 1: 14.4 (BU AC=1)
Solubility In Water: ING 1: COMPLETE 100%

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Fire and Explosion Hazard Data

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Flash Point: 0F,-17C
Flash Point Method: CC
Lower Explosive Limit: 2.5%
Upper Explosive Limit: 13%
Extinguishing Media: USE ALCOHOL FOAM, DRY CHEMICAL OR CARBON DIOXIDE

Ingredient: 5-NORBORNENE-2,3-DIMETHANOL,1,4,5,6,7,7,-HEXACHLORO-, CYCLIC SULFITE,ENDO-; (ALPHA - ENDOSULFAN) (SARA III)
Ingredient Sequence Number: 13
Percent: <0.1
NIOSH (RTECS) Number: RB9275100
CAS Number: 959-98-8
OSHA PEL: 0.1 MG/M3, S
ACGIH TLV: 0.1 MG/M3, S

Proprietary: NO
Ingredient: 5-NORBORNENE-2,3-DIMETHANOL,1,4,5,6,7,7-HEXACHLORO-, CYCLIC SULFITE,EXO-; (BETA - ENDOSULFAN) (SARA III)
Ingredient Sequence Number: 14
Percent: <0.1
NIOSH (RTECS) Number: RB9875200
CAS Number: 33213-65-9
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: 5-NORBORNENE-2,3-DIMETHANOL,1,4,5,6,7,7-HEXACHLORO-, CYCLIC SULFATE; (ENDOSULFAN SULFATE) (SARA III)
Ingredient Sequence Number: 15
Percent: <0.1
NIOSH (RTECS) Number: RB9150000
CAS Number: 1031-07-8
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: 4,7-METHANOINDANE,1,2,4,5,6,7,8,8- OCTACHLORO-3A,4,7,7A-TETRAHYDRO-; (CHLORDANE) (SARA III)
Ingredient Sequence Number: 16
Percent: <0.1
NIOSH (RTECS) Number: PB9800000
CAS Number: 57-74-9
OSHA PEL: 0.5 MG/M3, S
ACGIH TLV: 0.5 MG/M3, S

Proprietary: NO
Ingredient: ENDRIN ALDEHYDE (SARA III)
Ingredient Sequence Number: 17
Percent: <0.1
NIOSH (RTECS) Number: 1007497EA
CAS Number: 7421-93-4
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: ING 7:(ENDRIN) (SARA III)
Ingredient Sequence Number: 08
NIOSH (RTECS) Number: 9999999ZZ
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: 4,7-METHANOINDANE, 1,4,5,6,7,8,8-HEPTACHLORO-3A, 4,7,7A-TETRAHYDRO-; (HEPTACHLOR) (SARA III)
Ingredient Sequence Number: 09
Percent: <0.1
NIOSH (RTECS) Number: PC0700000
CAS Number: 76-44-8
OSHA PEL: 0.5 PPM, S
ACGIH TLV: 0.5 PPM, S

Proprietary: NO
Ingredient: 4,7-METHANOINDANE, 1,4,5,6,7,8,8-HEPTACHLORO-2, 3-EPOXY-3A,4,7,7A-TETRAHYDRO-; (HEPTACHLOR EPOXIDE) (SARA III)
Ingredient Sequence Number: 10
Percent: <0.1
NIOSH (RTECS) Number: PB9450000
CAS Number: 1024-57-3
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: CYCLOHEXANE,1,2,3,4,5,6-HEXACHLORO-, GAMMA-ISOMER; (LINDANE) (SARA III)
Ingredient Sequence Number: 11
Percent: <0.1
NIOSH (RTECS) Number: GV4900000
CAS Number: 58-89-9
OSHA PEL: 0.5 MG/M3, S
ACGIH TLV: 0.5 MG/M3, S

Proprietary: NO
Ingredient: 1,4:5,8-DIMETHANONAPHTHALENE,1,2,3,4,10,10- HEXACHLORO-1,4,4A,5,8,8A-HEXAHYDRO-,ENDO,EXO-; (ALDRIN) (SARA III)
Ingredient Sequence Number: 12
Percent: <0.1
NIOSH (RTECS) Number: IO2100000
CAS Number: 309-00-2
OSHA PEL: 0.025 MG/M3, S
ACGIH TLV: 0.025 MG/M3, S

Proprietary: NO

Proprietary: NO
Ingredient: ETHANE, 1,1-DICHLORO-2, 2-BIS(P-CHLOROPHENYL)-; (DDD) (SARA III)
Ingredient Sequence Number: 03
Percent: <0.1
NIOSH (RTECS) Number: KI0700000
CAS Number: 72-54-8
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: ETHANE,1,1,1-TRICHLORO-2,2-BIS(P-CHLOROPHENYL)-; (DDT) (DICHLORODIPHENYLTRICHLOROETHANE) (SARA III).
Ingredient Sequence Number: 04
Percent: <0.1
NIOSH (RTECS) Number: KJ3325000
CAS Number: 50-29-3
OSHA PEL: 1 MG/M3, S
ACGIH TLV: 1 MG/M3

Proprietary: NO
Ingredient: 1,4:5,8-DIMETHANONAPHTHALENE, 1,2,3,4,10,10- HEXACHLORO-6, 7-EPOXY-1,4,4A,5,6,7,8,8A- OCTAHYDRO,ENDO,EXO-; (ING 6)
Ingredient Sequence Number: 05
Percent: <0.1
NIOSH (RTECS) Number: IO1750000
CAS Number: 60-57-1
OSHA PEL: 0.25 MG/M3, S
ACGIH TLV: 0.25 MG/M3, S

Proprietary: NO
Ingredient: ING 5:(DIELDRIN) (SARA III)
Ingredient Sequence Number: 06
NIOSH (RTECS) Number: 9999999ZZ
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Proprietary: NO
Ingredient: 1,4:5,8-DIMETHANONAPHTHALENE, 1,2,3,4,10,10- HEXACHLORO-6, 7-EPOXY-1,4,4A,5,6,7,8,8A- OCTAHYDRO-,ENDO,ENDO-; (ING 8)
Ingredient Sequence Number: 07
Percent: <0.1
NIOSH (RTECS) Number: IO1575000
CAS Number: 72-20-8
OSHA PEL: 0.1 MG/M3, S
ACGIH TLV: 0.1 MG/M3, S

EXtension TOXicology NETwork
Information about this particular compound
FDA Pestrak files
Data Base of the Occurrence and Distribution of Pesticides in Chesapeake Bay
Information about this particular compound
Pesticide Leachability
Herbicide Mode-of-Action Summary
The ARS Pesticide Properties Database
Information about this particular compound
USEPA / OPP's Chemical Ingredients Database
Information about this particular compound
US EPA Status of Pesticides in Registration (in PDF format)
Florida Agricultural Information Retrieval System
Information about this particular compound
Applied Agricultural Chemicals
Characteristics of pesticides

Physical Properties

Environmental Science Center database with Experimental Log P coefficients etc.
Information about this particular compound
NIST Chemistry WebBook
Information about this particular compound
Pollution Prevention Progress Measurement Method (3P2M) Hazard Ranking
Spectrum Laboratories, Inc.
Information about this particular compound

Regulations

NASA Department of Environmental Services List Of Lists of Regulated Chemicals
Information about this particular compound

ACX Number	X1003134-4	CAS RN	330-55-2
Melting Point (°C)	93 - 94	Density	
Boiling Point (°C)	180 - 190	Vapor Density	
Refractive Index		Vapor Pressure	
Evaporation Rate		Water Solubility	0.0075 g/100
Flash Point (°C)		EPA Code	
DOT Number		RTECS	YS9100000
Comments			

More information about the chemical is available in these categories:

Biochemistry | Health | Misc | Pesticides/Herbicides
Physical Properties | Regulations | Structures

Biochemistry

Chemicals Inspection and Testing Service, Japan: Biodegradation and Bioaccumulation Data of Existing Ch
Information about this particular compound

Health

RAIS Nonradionuclides Toxicity Values

International Toxicity Estimates for Risk
Information about this particular compound

8(e) TRIAGE Chemical Studies Database

UMCP Partial list of mutagens

Australian Hazardous Substances Database
Information about this particular compound

Misc

USGS National Water Quality Laboratory (NWQL) schedules

Protocol Analytical Supplies, Inc. Single-component standards

Pesticides/Herbicides

ANALYTICAL PRODUCTS GROUP -- PESTICIDES QC STANDARD
MATERIAL SAFETY DATA SHEET
NSN: 664000N043979
Manufacturer's CAGE: 0HWA6
Part No. Indicator: A
Part Number/Trade Name: PESTICIDES QC STANDARD

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General Information

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Company's Name: ANALYTICAL PRODUCTS GROUP INC
Company's Street: 2730 WASHINGTON BLVD
Company's City: BELPRE
Company's State: OH
Company's Country: US
Company's Zip Code: 45714
Company's Emerg Ph #: 800-272-4442
Company's Info Ph #: 614-423-4200
Record No. For Safety Entry: 001
Tot Safety Entries This Stk#: 001
Status: SMJ
Date MSDS Prepared: 01OCT91
Safety Data Review Date: 27NOV95
MSDS Preparer's Name: T.V.C.
Preparer's Company: SAME
MSDS Serial Number: BTLQQ
Hazard Characteristic Code: F5

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Ingredients/Identity Information

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Proprietary: NO
Ingredient: ACETONE (SARA III). BP:132F,56C. SP GR:0.79 (H*2O=1). VP:181 @ 20C. MP:-139F,-95C. VAP DENS:2.
Ingredient Sequence Number: 01
Percent: >99
NIOSH (RTECS) Number: AL3150000
CAS Number: 67-64-1
OSHA PEL: 750PPM;1000 PPM STEL
ACGIH TLV: 750PPM;1000 PPM STEL

Proprietary: NO
Ingredient: ETHYLENE, 1,1-DICHLORO-2, 2-BIS(P-CHLOROPHENYL)-; (DDE) (SARA III)
Ingredient Sequence Number: 02
Percent: <0.1
NIOSH (RTECS) Number: KV9450000
CAS Number: 72-55-9
OSHA PEL: N/K (FP N)
ACGIH TLV: N/K (FP N)

Chemicals Being Added to the EPCRA Section 313 List

California EPA List of Lists

Substances in IRIS (Integrated Risk Information System) (main EPA site)

Information about this particular compound

Title III List of Lists

Current List of Toxics Release Inventory Chemicals

OSHA Chemical Sampling and Methods

Information about this particular compound

Guide to EPA Air Sampling Standards

Information about this particular compound

Information about this particular compound

Guide to NIOSH/OSHA Air Sampling Methods

Information about this particular compound

Information about this particular compound

Structures

GIF images of some pesticides

Information about this particular compound

Enter a chemical name, CAS Number, molecular formula, or molecular weight

New Search

Substructure Query with Plug-In or Substructure Query with Java

MSDS for Finasteride and Phenobarbital will be added when received.

EPA Contract No. 68-W-01-023 (Battelle Prime Contractor)
RTI Contract No.: 65U-08055.001.015.001
RTI Master Protocol No.: RTI- 831
RTI Study Code: Rt02-ED03

Amendment 1 **4/17/03**

TITLE: Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 Through 52/53

SPONSOR: Battelle Memorial Institute
505 King Avenue
Columbus, OH 43201-2693

TESTING FACILITY: RTI International
Chemistry and Life Sciences
Center for Life Sciences and Toxicology
Post Office Box 12194
Research Triangle Park, NC 27709

Study Protocol RTI-831, is hereby amended as indicated below (changes are **bolded** for clarity).

Item 1

Approval page, page 2:

The designation of David P. Houchens, Ph.D. is hereby changed from Principal Investigator/Program Manager to **Program Manager**.

Justification: Correction of an error in the project role designation of David P. Houchens.

Item 2

Section 2.1, Test Substances, page 7, which reads:

"2.1 TEST SUBSTANCES

2.1.1 Atrazine
CAS Number 1912-24-9

2.1.2 Propylthiouracil
CAS Number 51-52-5

2.1.3 Vinclozolin
CAS Number 50471-44-8

2.1.4 Linuron
CAS Number 330-55-2

2.1.5 p,p-DDE
CAS Number 72-55-9

2.1.6 Ketoconazole
CAS Number 65277-42-1

2.1.7 Methoxychlor

CAS Number 72-43-5

2.1.8 Finasteride

CAS Number 98319-26-7

2.1.9 Phenobarbital

CAS Number 50-06-6

is hereby amended to read:

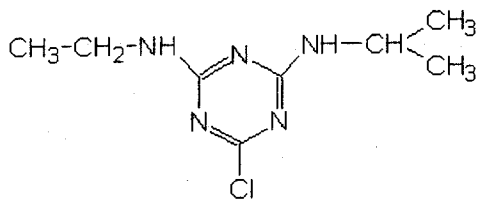
"2.0 MATERIALS AND METHODS

2.1 TEST SUBSTANCES

2.1.1 Atrazine
CAS Number: 1912-24-9

Synonyms: Weedex; Cyazine; Candex; 2-Chloro-4-(isopropylamino)-6-ethylamino-s-triazine; 1-Chloro-3-ethylamino-5-isopropylamino-2,4,6-triazine; Azinotox 500; Radazine; Fenatrol; Atrazine; Atrex; Atratol; Primatol A; 6-chloro-N-ethyl-N'-isopropyl-1,3,5-triazine-2,4-diamine; A 361; aatrex; hungazin; aktinit a; 2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine; g 30027; gesaprim; Atranex; Vectal SC; Crisamina; Scotts Bonus Type S; Crisazina; Vectral SC; Attrex; Ortho St. Augustine Weed and Feed; Griffex 4L; Atrazine 4L; Atrazine 80W; AAtrex 80W; AAtrex 4L; ATZ; 2-Chloro-4-(2-propylamino)-6-ethylamino-s-triazine; Atrazines; Laddock; Extrazine II; Fogard; Griffex; Mebazine; Vectal; weedex a; zeaphos; aktikon pk; aktinit pk; Wonuk; oleogesaprim; chromozin; pitezin; actinite pk; gesaprim 50; akticon; atrataf; zeapos; oleogesaprim 200; gesaprim 500; maizina; aatrex nine-o; atazinax; atrasine; atratol a; Atred; cekuzina-t; 2-chloro-4-ethylamino-6-isopropylamino-s-triazine; crisatrina; crisazine; farmco atrazine; fenamine; geigy 30,027; gesoprim; inakor; primatol; primaze; radizine; strazine; hungazin pk; triazine a 1294;zeazin;argezin;aktikon;

Structure:



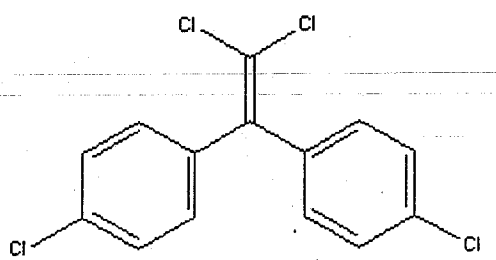
Supplier:	**Chem Services.**
Lot. No.	**285-63B**
Purity:	**98%**
Appearance:	**Crystalline solid**
Molecular Formula:	**C8H14ClN5**
Molecular Weight:	**215.72**
Storage, Bulk Chemical:	**Room Temperature**
Storage, Test Solution:	**4 deg C**

2.1.2 p,p-DDE

CAS Number: **72-55-9**

Synonyms: p,p'-DDE; DDE; 4,4'-DDE; Dichlorodiphenyldichloroethylene; 2,2-bis(p-chlorophenyl)-1,1-dichloroethene; ddt dehydrochloride; p,p'-dichlorodiphenyl dichloroethylene; 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene; 2,2-bis(4-chlorophenyl)-1,1-dichloroethylene; p,p'-Dichlorodiphenyldichloroethylene (DDE) ; p,p-DDE; P,P'-DICHLORODIPHENYLDICHLOROETHYLENE (DDE); p,p[-DDE;

Structure:



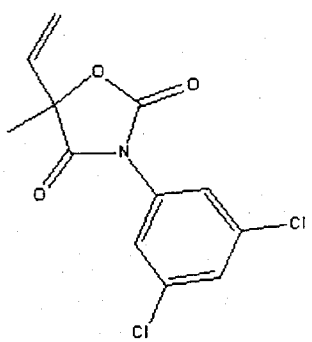
Supplier:	**Sigma**
Lot. No.:	**09020KU**
Purity:	**98.6%**
Appearance:	**White crystals**
Molecular Formula:	**C14H8Cl4**
Molecular Weight:	**318.03**
Storage, Bulk Chemical:	**Room Temperature**
Storage, Test Solution.:	**4 deg C**

2.1.3 Vinclozolin

CAS Number: **50471-44-8**

Synonyms: Vorlan; 3-(3,5-Dichlorophenyl)-5-methyl-5-vinyl-2,4-oxazolidinedione; Ornalin; Oxazolidinedione, 3-(3,5-dichlorophenyl)-5-ethenyl-5-methyl-; Vinclozolin; Ronilan; vinclozalin; 3-(3,5-Dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione; VINCLOZOLIN [RONILAN]; Vinclozolin ; 3-(3,5-dichlorophenyl)-5-methyl-5-vinyl-1,3-oxazolidine-2,4-dione;

Structure:



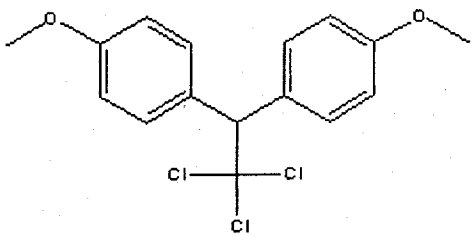
Supplier:	**Chem Services.**
Lot No:	**281-54A**
Purity:	**99.0%**
Appearance:	**Crystalline solid**
Molecular Formula:	**C12H9Cl2NO3**
Molecular Weight:	**286.12**
Storage, Bulk Chemical:	**Room Temperature**
Storage, Test Solution:	**4 deg C**

2.1.4 Methoxychlor

CAS Number: 72-43-5

Synonyms: 1,1'-(2,2,2-Trichloroethylidene)-bis[4-methoxybenzene]; 1,1,1-trichloro-2,2-bis(p-methoxyphenyl)ethane; Methoxychlor; 2,2-bis(p-methoxyphenyl)-1,1,1-trichloroethane; Marlate; Metox; Chemform; DMDT; Methoxy DDT; Maxie; Maralate; 2,2-bis(p-anisyl)-1,1,1-trichloroethane; 1,1-bis(p-methoxyphenyl)-2,2,2-trichloroethane; dianisyltrichloroethane; p,p'-dimethoxydiphenyltrichloroethane; di(p-methoxyphenyl) trichloromethyl methane; 2,2,2-trichloro-1,1-bis(4-methoxyphenyl)ethane; dimethoxy-ddt; methoxcide; methoxo; dimethoxy-dt; p,p'-dmdt; flo pro mcseed protectant; p,p'-methoxychlor; Moxie; oms 466; 4,4-(2,2,2-trichloroethylidene)dianisole; double-m ec; methoxychlor 2 ec; mezox k; 1,1,1-Trichloro-2,2-bis(p-anisyl)ethane; Bis(p-anisyl)-1,1,1-trichloroethane; Bis(p-methoxyphenyl)-1,1,1-trichloroethane; Dimethoxydiphenyltrichloroethane; Chemform methoxychlor;

Structure:

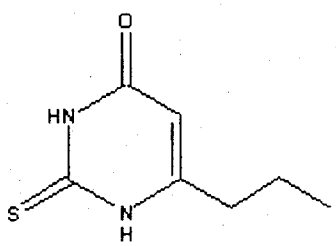


Supplier:	Sigma
Lot Number:	49H1328
Purity:	95.2%
Appearance:	Light orange powder
Molecular Formula:	C16H15Cl3O2
Molecular Weight:	345.7
Storage, Bulk Chemical:	Room Temperature
Storage, Test Solution:	4 deg C

2.1.5 Propylthiouracil
CAS Number" 51-52-5

Synonyms: 4-hydroxy-2-mercapto-6-propylpyrimidine; 6-n-propyl-2-thiouracil; procasil; propacil; propycil; 6-propyl-2-thiopyrimidine-2,4(1H,3H)-dione; 6-propylthiouracil; prothyran; thyreostat propyl-thyracil; prothiurone; prothycil; protiural; propyl-thiorist; propylthiorit; thiuragyl; prothiucil; ptu(thyreostatic); 2-mercapto-6-propylpyrimid-4-one; thyreostat ii; T 72; 2,3-dihydro-6-propyl-2-thioxo-4(1H)-Pyrimidinone; 6-Propyl-2-thiouracil;

Structure:

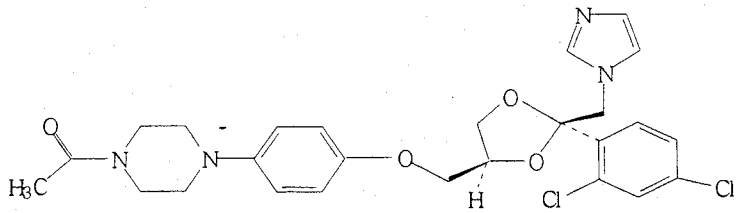


Supplier:	TCI
Lot Number:	GF01
Purity:	99.0%
Appearance:	White Powder
Molecular Formula:	C7H10N2OS
Molecular Weight:	170.23
Storage, Bulk Chemical:	Room Temperature
Storage, Test Solution:	4 deg C

2.1.6 Ketoconazole
CAS Number : 65277-42-1

Synonyms: Fungarest; Fungarol; Ketoderm; Ketoisdin; Orifungal M; Panfungol; Fungoral; Ketoconazole; Nizoral; cis-1-acetyl-4-(4-((2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl)methoxy)phenyl)piperazine;

Structure:



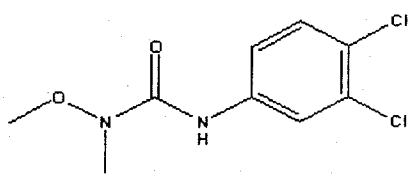
Supplier:	**Spectrum Quality Products**
Lot Number:	**K1149**
Purity:	**99.83%**
Appearance:	**solid**
Molecular Formula:	**C26H28Cl2N4O4**
Molecular Weight:	**531.48**
Storage, Bulk Chemical:	**Room Temperature**
Storage, Test Solution:	**4 deg C**

2.1.7 Linuron

CAS Number: **330-55-2**

Synonyms: Linuron ; N-(3,4-Dichlorophenyl)-N'-methoxy-N'-methylurea; Linuron; Lorox; Afalon; Linurex; N'-(3,4-Dichlorophenyl)-N-methoxy-N-methylurea; methoxydiuron; du Pont Herbicide 326; Hoe 2810; Linorox; Sarclex; Aflon; Linex 4L; Lorox 4L; Lorox 50W; Lorox DF; Lorox L; Lorox Plus; Alafon; Linex; Lorax; 1-Methoxy-1-methyl-3-(3,4-dichlorophenyl)urea; 3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea; Urea, 1-(3,4-dichlorophenyl)-3-methoxy-3-methyl-; Garnitan; Methoxy-1-methyl-3-(3,4-dichlorophenyl)urea; Premalin; Cephalon; 3-(3,4-Dichlorophenyl)-1-methoxy(methyl)urea;

Structure:



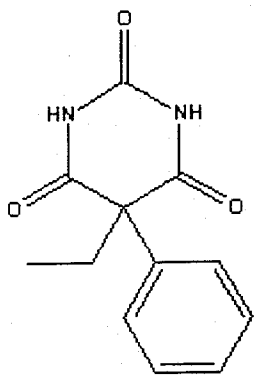
Supplier:	**Chem Services**
Lot Number:	**273-81B**
Purity:	**99%**
Appearance:	**Crystalline solid**
Molecular Formula:	**C9H10Cl2N2O2**
Molecular Weight:	**249**
Storage, Bulk Chemical:	**Room Temperature**
Storage, Test Solution:	**4 deg C**

2.1.8 Phenobarbital

CAS Number: 50-06-6

Synonyms: Tedral; Donnazyme; Donphen; Antrocol; Arco-Lase Plus; Gustase-Plus; Pamine PB; SK-Phenobarbital; Phazyme-PB; Valprin 50-PB; barbita; Solfoton; Phenobarbitone; Phenylethylbarbituric acid; 5-Ethyl-5-phenylbarbituric acid; Adonal; Luminal; Nunol; Phenobarbital; 5-ethyl-5-phenyl-2,4,6-(1H,3H,5H)pyrimidinetrione; phenobarbituric acid; 5-phenyl-5-ethylbarbituric acid; phenylethylmalonylurea; phenylethylbarbiturate; aephenal; agrypnal; amylofene; aphenylbarbit; aphenyletten; austrominal; barbapil; barbellen; barbellon; barbenyl; barbilehae; barbinal; barbiphen; barbiphenyl; barbipil; barbivis; barbonal; barbophen; bardorm; bartol; bialminal; blu-phen; cabronal; calmetten; calminal; cardenal; codibarbita; coronaletta; cratecil; damoral; dezibarbitur; dormina; dormiral; doscalun; duneryl; ensobarb; ensodorm; epanal; epidorm; epilol; episedal; epsylone; eskabarb; etilfen; euneryl; fenbital; fenemal; fenobarbital; fenosed; fenylettae; gardenal; gardepanyl; glysoletten; haplopan; haplos; helional; hennoletten; hypnaletten; hypnogen; hypnolone; hypnoltol; hypno-tablinetten; hysteps; lefebar; leonal; lephebar; lepinal; lepinaletten; linasen; liquital; lixophen; lubergal; lubrokal; Lumen; lumesettes; lumesyn; lumofridetten; luphenil; luramin; molinal; neurobarb; nirvonal; noptil; nova-pheno; parkotal; pharmetten; phen-bar; phenemal; phenemalum; phenobal; phenobarb; phenobarbitalum; phenobarbyl; phenoluric; phenomet; phenonyl; phenyletten; phenylral; PHOB; polcominal; promptonal; sedabar; seda-tablinen; sedicat; sedizorin; Sedlyn; sedofen; sedonal; sedonettes; sedophen; sevenal; sombutol; somnolens; somnoletten; somnosan; somonal; spasepilin; starifen; starilettae; stental; stental extentabs; talpheno; teolaxin; teoloxin; theoloxin; theominal; triabarb; tridezibarbitur; triphenatol; versomnal; zadoletten; zadonal; Phenobarbitol; Barbipenyl;

Structure:

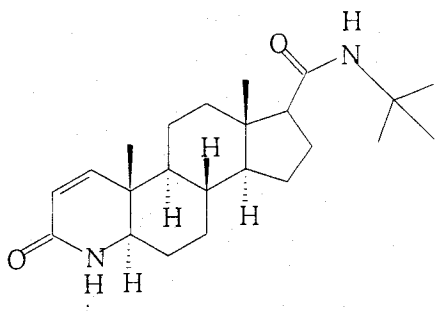


Supplier:	**Sigma**
Lot Number:	**81K2620**
Purity:	**98%**
Appearance:	**Powder**
Molecular Formula:	**C12H12N2O3**
Molecular Weight:	**232.2**
Storage, Bulk Chemical:	**4 deg C**
Storage, Test Solution:	**4 deg C**

2.1.9 Finasteride

CAS Number: **98319-26-7**

Synonyms: Finasteride; Proscar;
Structure:



Supplier:	**Merck**
Lot Number:	**TBD**
Purity:	**TBD**
Appearance:	**TBD**
Molecular Formula:	**C23H36N202**
Molecular Weight:	**372.55**
Storage, Bulk Chemical:	**TBD**
Storage, Test Solution:	**TBD**

Note: Aquisition of finasteride by the sponsor from the supplier has been delayed . Testing of finasteride using the study design described in this protocol, if scheduled, will take place at a later time.

Justification: Addition of chemical information that was not included and/or not available when the protocol was written.

Item 3

Section 2.3, DOSE FORMULATION AND ANALYSIS, page 8, which reads:

"The dosing suspensions will be prepared at a frequency determined by stability tests performed prior to the start of the study. Suspensions will be prepared at Battelle Chemical Repository, Sequim, WA, and stored in wide-mouth, amber bottles. They will be shipped via 24-hour express delivery and logged into the RTI Materials Handling Facility prior to transfer to the Reproductive and Developmental Toxicology Laboratory for dosing. The test materials will be suspended in stripped (α-tocopherol [Vitamin E] removed) Mazola® corn oil (CAS No. 8001-30-7), with the concentration determined by the following formula:

$$\text{Concentration (mg / ml)} = \frac{\text{Dose per time (mg / kg)}}{\text{Dosage volume per time (5.0 ml / kg)}}$$

An aliquot of each dose level per formulation will be analyzed by Battelle. The dosing bottles will be identified at RTI by a five-digit random number Rx code, and a color code. Personnel, other than the Laboratory Supervisor, Project Toxicologist, and Study Director, will not be informed of the test chemicals or formulation concentrations until all laboratory work is completed (i.e., the study technicians will be "blind" for chemical and dose). Aliquots from the dosing bottles will be collected on the first day of dosing (postnatal day [pnd] 23) and on the first pnd 30, 37, 44, and 51 and will be shipped to Battelle Chemical Repository, Sequim, WA, for analysis."

is hereby amended to read:

2.3 DOSE FORMULATION AND ANALYSIS

"The dosing suspensions/**solutions** will be prepared at a frequency determined by stability tests **initiated** prior to the start of the study. Suspensions/**solutions** will be prepared at **the** Battelle Chemical Repository, Sequim, WA, and stored in wide-mouth, **200 ml** amber bottles. They will be shipped **on ice or with frozen cold packs** via 24-hour express delivery and logged into the RTI Materials Handling Facility. Prior to transfer to the Reproductive and

Developmental Toxicology Laboratory for dosing **the concentration of the dose formulations will be verified by the Battelle Chemical Respository**. The test materials will be suspended/**dissolved** in Mazola® corn oil (CAS No. 8001-30-7), with the concentration determined by the following formula:

$$\text{Concentration (mg / ml)} = \frac{\text{Dose per time (mg / kg)}}{\text{Dosage volume per time (5 ml / kg)}}$$

An aliquot of each dose level per formulation will be analyzed by Battelle. The dosing bottles will be identified at RTI by a five-digit random number Rx code, and a color code. Personnel, other than the Laboratory Supervisor, Project Toxicologist, and Study Director, will not be informed of the test chemicals or formulation concentrations until all laboratory work is completed (i.e., the study technicians will be "blind" for chemical and dose). **The dosing formulations will be stored at refrigerated temperatures. Prior to dosing each day, the formulations will be removed from the refrigerator. Solutions will be shaken and warmed to room temperature. Suspensions will be placed on a stir plate, and stirred and warmed to room temperature.** Aliquots **(at least 5 milliliters)** from the dosing bottles will be collected on the first day of dosing (**the first** postnatal day [pnd] **23**) and on the first pnd 30, 37, 44, and 51. **These samples will be held in refrigerated storage until the end of the dosing period, when they will be shipped overnight on frozen cold packs to** Battelle Chemical Repository, Sequim, WA, for analysis."

Justification: To add information describing the procedures for sample volume, storage, and shipping conditions for the dose formulations that was not available at the time of protocol approval. Evaluation of chemical/corn oil mixtures indicated that some were solutions and some were suspensions (e-mail from D. Houchens, 06/07/02, and J. Johnson, 06/12/02). Storage conditions and mixing procedures for the dose formulations were discussed in a conference call with J. Johnson (Battelle, Columbus) and E. Crecelius (Battelle, Sequim) on 09/03/02. Dose administration procedures followed SOP TERA 106.7. In addition, effective 6/13/02, the vehicle was changed to plain corn oil. The precision of the dose volume was corrected.

Item 4

Section 2.4.3, Total Number, Age, and Weight, page 9, which reads:

"For the nine-group component of this study (Component 1; see Table 1), 25 timed-pregnant female rats (designated the F0 generation) will be purchased for this study, at ten to 12 weeks of age upon

arrival. They will arrive at RTI on gestational day (gd) 14 (based on the vendor's designation of the day of insemination as gd 1), which is gd 13 (based on the performing laboratory's designation of the day of insemination as gd 0). One hundred thirty-five (135) offspring male rats, designated the F1 generation, will be placed on study at weaning (pnd 21), weighing approximately 48-55 grams (i.e., nine groups of 15 F1 weanling males each), for Component 1. For the 11-group component of this study (Component 2; see Table 1), 32 timed-pregnant female rats will be purchased, as described above, and 165 offspring male rats (11 groups of 15 F1 weanling males each) will go on study for Component 2."

is hereby amended to include the following sentence at the end of the section:

"For **each** nine-group components of this study (see Table 1), 25 timed-pregnant female rats (designated the F0 generation) will be purchased for this study, at ten to 12 weeks of age upon arrival. They will arrive at RTI on gestational day (gd) 14 (based on the vendor's designation of the day of insemination as gd 1), which is gd 13 (based on the performing laboratory's designation of the day of insemination as gd 0). One hundred thirty-five (135) offspring male rats, designated the F1 generation, will be placed on study at weaning (pnd 21), weighing approximately 48-55 grams (i.e., nine groups of 15 F1 weanling males each), for **each component**. **In addition, two non-pregnant female rats, 10-12 weeks of age will be ordered for each component, from the same animal room at the supplier as the pregnant animals, to be assigned as quality control animals."**

Justification: The number of treatment groups changed in Component 2, and the animals to be used for quality control were not specified in this section of the protocol.

Item 5

Section 2.4.4, Quality Control, page 9, which reads:

"The shipment of pregnant females will be quarantined on arrival, and quality control evaluation will be initiated within one day after receipt. Within one day after receipt, two female rats will be chosen from the shipment, sacrificed, and blood collected for assessment of viral antibody status. Heat-inactivated serum will be sent to BioReliance (Rockville, MD) for their Level 1 Rat Antibody Screen. The viral screen will consist of evaluation for the presence of antibodies against the following: Toolan H-1 virus (H-1), Sendai virus, Pneumonia virus of mice (PVM), rat coronavirus/sialodacryoadenitis (RCV/SDA), Parvo virus, Kilham rat virus (KRV), CAR Bacillus, and Mycoplasma pulmonis (*M. Pul.*). In

addition, fecal samples from representative animals will be externally examined for intestinal parasites."

is hereby amended as follows:

"The shipment of pregnant **and two non-pregnant** females will be quarantined on arrival, and quality control evaluation will be initiated within one day after receipt. Within one day after receipt, the two **non-pregnant** female rats will be sacrificed, and blood collected for assessment of viral antibody status. Heat-inactivated serum will be sent to BioReliance (Rockville, MD) for their Level 1 Rat Antibody Screen. The viral screen will consist of evaluation for the presence of antibodies against the following: Toolan H-1 virus (H-1), Sendai virus, Pneumonia virus of mice (PVM), rat coronavirus/sialodacryoadenitis (RCV/SDA), Parvo virus, Kilham rat virus (KRV), CAR Bacillus, and Mycoplasma pulmonis (*M. Pul.*). In addition, fecal samples from representative animals will be externally examined for intestinal parasites.

Justification: Selection of the non-pregnant animals for quality control was not clearly specified.

Item 6

Section 2.5.1, Housing, Feed, and Water, page 10,which reads:

"During the quarantine period, animals will be randomly assigned to cages. Pregnant and lactating females will be singly housed, and F1 male postweanlings will be multiply, or singly housed, as necessary, in solid-bottom, polycarbonate cages (8"x19"x10.5") fitted with stainless steel wire lids (Laboratory Products, Rochelle Park, NJ). Sani-Chip® cage bedding (P.J. Murphy, Forest Products, Inc., Montville, NJ) will be used in all cages. Pelleted feed (No. 5002 Purina Certified Rodent Chow®) and deionized water, produced at RTI from tap water from the Durham, NC, water system, in plastic bottles with stainless-steel sipper tubes, will be available *ad libitum* for the F0 females during quarantine, gestation and lactation, and for the retained F1 mmales. The water for the study breeder male animals is provided by an automatic watering system (Edstrom Industries, Inc., Waterford, WI); the parental females will also be on the automatic watering system during cohabitation. The analysis of the rodent chow for chemical composition and possible chemical contamination, and analysis of Durham City water will be provided by the suppliers and maintained in the study records. It

is anticipated that contaminant levels will be below certified levels for both feed and water and will not affect the design, conduct, or conclusions of this study. In addition, each lot number of Purina 5002 feed used will be analyzed by the supplier for concentrations of the phytoestrogens genistein, daidzein, and glycitein. An aliquot of each lot number will be retained frozen for possible future analytical chemistry. The "metabolizable energy content" of the feed (label value) will also be recorded and reported. Rat chow will be stored at approximately 60-70°F, and the period of use will not exceed six months from the milling date. At all times, animals will be housed, handled, and used according to the NRC Guide (NRC, 1996)."

is hereby amended as follows:

"During the quarantine period, animals will be randomly assigned to cages. Pregnant and lactating **F0** females will be singly housed, and F1 male postweanlings will be singly housed in solid-bottom, polycarbonate cages (8"x19"x10.5") fitted with stainless steel wire lids (Laboratory Products, Rochelle Park, NJ). Sani-Chip® cage bedding (P.J. Murphy, Forest Products, Inc., Montville, NJ) will be used in all cages. Pelleted feed (No. 5002 Purina Certified Rodent Chow®) and deionized water, produced at RTI from tap water from the Durham, NC, water system, in plastic bottles with stainless-steel sipper tubes, will be available *ad libitum* for the F0 females during quarantine, **for the F0 females during gestation and lactation,** and for the retained F1 males. The analysis of the rodent chow for chemical composition and possible chemical contamination, and analysis of Durham City water will be provided by the suppliers and maintained in the study records. It is anticipated that contaminant levels will be below certified levels for both feed and water and will not affect the design, conduct, or conclusions of this study. In addition, each lot number of Purina 5002 feed used will be analyzed by the supplier for concentrations of the phytoestrogens genistein, daidzein, and glycitein. An aliquot of each lot number will be retained frozen for possible future analytical chemistry. The "metabolizable energy content" of the feed (label value) will also be recorded and reported. Rat chow will be stored at approximately 60-70°F, and the period of use will not exceed six months from the milling date. At all times, animals will be housed, handled, and used according to the NRC Guide (NRC, 1996)."

Justification: The paragraph was edited to indicate that the weanling males will be singly housed, which is necessary if feed consumption is to be collected. The reference to the water supply for breeder males and cohabited females was removed, since vendor-bred pregnant animals were ordered for this study.

Item 7

Section 2.5.3, Animal Identification, page 11, which reads:

> "All F0 maternal rats will be individually identified by ear tag after arrival at RTI. All selected study weanling F1 males will also be uniquely identified by eartag at weaning, as well as receiving a female study number. All data generated during the course of this study will be tracked by these numbers."

is hereby amended to read:

All F0 maternal rats will be individually identified by ear tag after arrival at RTI, **as well as receiving a female study number.** All selected study weanling F1 males will also be uniquely identified by eartag at weaning, as well as receiving an F1 **male** study number. All data generated during the course of this study will be tracked by these numbers.

Justification: Identification procedures for animals on study were clarified.

Item 8

Section 3.1, Study Design, Test Chemicals, and Dose Selection, page 11, paragraph 2, which reads:

> "The U.S. EPA selected the nine test chemicals for evaluation and selected the low and high target doses (in mg/kg/day) for each of them (Table 1). The nine test chemicals and their target/mechanism of action are as follows: (1) atrazine (affects the hypothalamus-pituitary axis in female rats and ovulation); (2) propylthiouracil (affects the thyroid directly, causing hypothyroidism); (3) vinclozolin (metabolites M1 and M2 act as anti-androgen; competitive binding to androgen receptor; M1 also binds weakly to the rat progesterone receptor); (4) linuron (anti-androgen; competitive binding to androgen receptor); (5) p,p-DDE (stable metabolite of DDT; anti-androgen through competitive binding to the androgen receptor); (6) ketoconazole (inhibits steroidogenesis in both sexes); (7) methoxychlor (a xeno-estrogen through α-estrogen receptor, anti-estrogen through β-estrogen receptor and an anti-androgen through androgen receptor mediated mechanism); (8) finasteride (a inhibitor of a 5α-reductase which catalyzes the conversion of testosterone to its potent metabolite, dihydrotestosterone [DHT]); and (9) phenobarbital (induces P450 isoforms

predominantly in the liver, accelerates metabolism of endogenous hormones and exogenous xenobiotics)."

is hereby amended to read:

"The U.S. EPA selected the nine test chemicals for evaluation and selected the low and high target doses (in mg/kg/day) for each of them (Table 1). The nine test chemicals and their target/mechanism of action are as follows: (1) atrazine (affects the hypothalamus-pituitary axis in female rats and ovulation); (2) p,p-DDE (stable metabolite of DDT; anti-androgen through competitive binding to the androgen receptor); (3) vinclozolin (metabolites M1 and M2 act as anti-androgen; competitive binding to androgen receptor; M1 also binds weakly to the rat progesterone receptor); (4) methoxychlor (a xeno-estrogen through α-estrogen receptor, anti-estrogen through β-estrogen receptor and an anti-androgen through androgen receptor mediated mechanism); (5) propylthiouracil (affects the thyroid directly, causing hypothyroidism); (6) ketoconazole (inhibits steroidogenesis in both sexes); (7) linuron (anti-androgen; competitive binding to androgen receptor); (8) phenobarbital (induces P450 isoforms predominantly in the liver, accelerates metabolism of endogenous hormones and exogenous xenobiotics); and (9) finasteride (a inhibitor of a 5α-reductase which catalyzes the conversion of testosterone to its potent metabolite, dihydrotestosterone [DHT])." **The availability of finasteride is still uncertain. Therefore, if tested, it could be done in a separate study with its own control group. The study design, test chemicals, and target doses are presented in Table 1."**

Justification: One of the test chemicals was not available in time to be included in the established study schedule for Component 2 (e-mail communication from D. Houchens, 05/10/02, 10/10/02) .

Item 9

Table 1, page 13, which reads:

Table 1. Study Design and Target Doses

Group No.	No. F1 Males	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)	Dose Volume (ml/kg)
			COMPONENT 1		
1	15	–[a]	0	0.0	5.0
2	15	Atrazine	75	15.0	5.0
3	15		150	30.0	5.0
4	15	Propylthiouracil	2	0.4	5.0
5	15		25	5.0	5.0
6	15	Vinclozolin	30	6.0	5.0
5	15		100	20.0	5.0
8	15	Linuron	50	10.0	5.0
9	15		100	20.0	5.0
			COMPONENT 2		
10	15	p,p'DDE	50	10.0	5.0
11	15		100	20.0	5.0
12	15	Ketoconazole	50	10.0	5.0
13	15		100	20.0	5.0
14	15	Methoxychlor	25	5.0	5.0
15	15		50	10.0	5.0
16	15	Finasteride	25	5.0	5.0
17	15		50	10.0	5.0
18	15	Phenobarbital	50	10.0	5.0
19	15		100	20.0	5.0
10	15	–[a]	0	0.0	5.0

[a] stripped corn oil, vehicle control

is hereby amended to read:

Table 1. Study Design, Test Chemicals and Target Doses

Group No.	No. F1Males	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)	Dose Volume (ml/kg)
			COMPONENT 1		
1	15	–[a]	0	0.0	5
2	15	Atrazine	75	15.0	5
3	15		150	30.0	5
4	15	p,p'DDE	50	10.0	5
5	15		100	20.0	5
6	15	Vinclozolin	30	6.0	5
7	15		100	20.0	5
8	15	Methoxychlor	25	5.0	5
9	15		50	10.0	5
			COMPONENT 2		
10	15	Propylthiouracil	2	0.4	5
11	15		25	5.0	5
12	15	Ketoconazole	50	10.0	5
13	15		100	20.0	5
14	15	Linuron	50	10.0	5
15	15		100	20.0	5
16	15	Phenobarbital	50	10.0	5
17	15		100	20.0	5
18	15	Finasteride[b]	25	5.0	5
19	15		50	10.0	5
20	15	–[a]	0	0.0	5

[a] corn oil, vehicle control

[b] Finasteride is still on the list of chemicals, but its availability is uncertain. If tested, it may be done in a separate study with its own control group.

Justification: Propylthiouracil and linuron were moved from Component 1 to Component 2 to allow more time for dose formulation analysis studies (see summary of conference call, 09/03/02). p,p'-DDE and methoxychlor were moved from Component 2 to Component 1 (see summary of conference call, 09/03/02). The testing status of finasteride was clarified (e-mail, 10/10/02). In addition, the correct vehicle was indicated, and the dosing volume was corrected for accuracy.

Item 10

Section 3.1, Study Design, Test Chemicals, and Dose Selection, Tentative Study Dates, page 12, which reads:

"**Tentative Study Dates**[a] (to be added to the protocol by amendment)

F0 timed-pregnant females arrive at RTI:

Parturition of F1 offspring (pnd 0):

Weaning of F1 offspring (pnd 21):

Sacrifice of F0 dams:

Dosing (pnd 23 - pnd 52/53):

Sacrifice of F1 females (on pnd 52 or 53)::

Submission of nonaudited draft final report:

Submission of audited draft final report:

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[a] The end dates are tentative and will depend on the duration of gestation and lactation of the F0 dams with F1 offspring."

is hereby amended to read:

Tentative Study Dates[a]

Component 1

Atrazine, p,p'-DDE, Vinclozolin, Methoxychlor

Receive 25 females at gd 13	**September 5, 2002**
Quarantine (gd 13-20)	**September 5 – 12, 2002**

PND 0	September 14, 15, 16, 2002
PND 21	October 5, 6, 7, 2002
Dosing Begins (PND 23)	October 7, 8, 9, 2002
PND 52	November 5, 6,7, 2002

Component 2

Propylthiouracil, Ketoconazole, Linuron, Phenobarbital, (Finasteride[b])

Receive 25 females at gd 13	Dec. 26, 2002
Quarantine (gd 13-20)	Dec. 26, 2002 to Jan. 2, 2003
1st PND 0	Jan 4, 2003
1st PND 21	Jan. 25, 2003
Receive Dose Formulations	Week of Jan 20, 2003
Dosing Begins (PND 23)	Jan. 28, 2003
1st PND 52	Feb. 26, 2003
Repro Organs/Thyroid Histopathology complete	April 11, 2003
Hormone Assays Complete	May 20, 2003
Notebooks to QA	June 3, 2003
Data Tables to Study Director/Data to QA	June 3, 2003
Internal draft report to QA	TBD
First draft QA'd report to Battelle	July 1, 2003

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[a] The end dates for the in-life portion of Component 2 are tentative and will depend on the duration of gestation and lactation of the F0 dams with F1 offspring.

[b]Finasteride is still on the list of chemicals, but its availability is uncertain. If tested, it may be done in a separate study with its own control group."

Justification

The actual study had not been scheduled when the protocol was signed. The current study schedule, insofar as it is known, is hereby entered into the protocol.

Item 11

Section 3.2.3.2, Standardization of Litter Sizes,page 15, which reads:

"On pnd 4, the size of each litter will be adjusted to ten pups, maximizing the number of male pups retained. Natural litters with ten or fewer pups will not be culled. If necessary, F1 male pups from litters with more than six males will be fostered to litters containing fewer than six males on pnd 4. All culled pups will be sacrificed by decapitation. The F0 dams will be allowed to rear their remaining F1 young to pnd 21. On pnd 21, each litter will be weaned."

is hereby amended to remove the sentence describing fostering F1 males, i.e., If necessary, F1 male pups from litters with more than six males will be fostered to litters containing fewer than six males on pnd 4.

Justification: Fostering of animals on pnd 4 would prevent valid use of pup weights collected on pnd 0 and 4 in conjunction with data after fostering on pnd 4.

Item 12

Section 3.4, Treatment of F1 Weanling Males, page 16, which reads:

"Beginning on pnd 23, each F1 male will be dosed with one of the test materials at one of the dose levels or the vehicle control (corn oil for all chemicals). Each animal will be weighed every other day prior to treatment and the body weight recorded. Treatments will be administered daily by oral gavage in 5.0 ml corn oil/kg body weight from pnd 23 and continuing through pnd 52/53. This duration of treatment is unnecessary to detect androgenic chemicals but is required for the detection of pubertal delay and antithyroid effects. Gavage dosing will use an 18-gauge gavage needle (1 inch length with 2.25 mm ball) and a 1 cc glass (disposable) tuberculin syringe for each treatment group. Xenobiotics will be administered in corn oil vehicle at a dosing volume of 5.0 ml/kg body weight at 0700-1000 hours daily. The treatments will be administered on a mg/kg body weight basis, adjusted based on the most recent body weight, and the volume of the dose administered will be recorded each day. It is important that any dosing solutions/suspensions be well mixed to keep the chemical in suspension prior to and throughout dosing.

is hereby amended to read:

"Beginning on pnd 23, each F1 male will be dosed with one of the test materials at one of the dose levels or the vehicle control (corn oil for all chemicals). Each animal will be weighed every other day prior to treatment and the body weight recorded. Treatments will be administered daily by oral gavage in **5 ml** corn oil/kg body weight from pnd 23 and continuing through pnd 52/53. This duration of treatment is unnecessary to detect androgenic chemicals but is required for the detection of pubertal delay and antithyroid effects. Gavage dosing will use an 18-gauge gavage needle (1 inch length with 2.25 mm ball) and a 1 cc glass **or plastic** (disposable) tuberculin syringe for each treatment group. **Xenobiotics will be administered beginning no earlier than 0700 hours daily, and continuing until all animals are dosed.** The treatments will be administered on a mg/kg body weight basis, adjusted based on the most recent body weight, and the volume of the dose administered will be recorded each day. It is important that any dosing solutions/suspensions be well mixed to keep the chemical in suspension prior to and throughout dosing.

Justification: The dose volume was changed to the correct accuracy. The use of either glass or plastic disposable tuberculin syringes as acceptable was designated. The period of time during which dosing is to occur was changed to allow a bigger window of time, since the previously allotted time was not sufficient.

Item 13

Section 3.6.2, Gross Necropsy and Organ Weights, page 17, first sentence, which reads:

"Each F1 male offspring, after blood is collected (see Section 3.7.1), will be subjected to a gross necropsy."

is hereby amended to read:

"Each F1 male offspring, after blood is collected (see Section **3.6.1**), will be subjected to a gross necropsy."

Justification: Correction of a typographical error.

Item 14

Section 3.6.3, Histology and Pathology, page 18, which reads:

"One testis, one epididymis, and the thyroid with attached portion of trachea from each F1 male will be placed in Bouin's fixative for 24 hours (then the trachea removed from the thyroid), after which they will be rinsed and stored in 70% alcohol until embedded in paraffin. They will then be sectioned at 3-5 microns and stained with hematoxylin and eosin (H and E) for subsequent histological evaluations. Optional tissues for histopathology include the liver, paired kidneys, adrenal glands (paired), and pituitary, as indicated by altered organ weight (change of "significant magnitude"), which will be processed as above. Stained sections will be evaluated by a Board Certified veterinary pathologist for pathologic abnormalities and potential treatment-related effects. Thyroids should be evaluated for morphologic changes such as altered follicular epithelial height, the relative number and staining characteristics of colloid, the extent of thyroid vascular supply, and the density, size, and shape of the thyroid follicles. The one testis and epididymis per male will be evaluated for spermatogenesis, spermiogenesis, status of seminiferous tubules in the testis, and sperm in the epididymis, as well as the structural integrity of these organs."

is hereby amended to read:

"**Tissues taken at necropsy will be placed in fixative and then transferred to Experimental Pathology Laboratories (EPL) for processing. The testes and epididymides from each F1 male will be placed in Bouin's fixative for 24 hours, after which they will be rinsed and stored in 70% alcohol until embedded in paraffin. The thyroid with attached portion of trachea will be fixed in 10% neutral buffered formalin. The thyroid (with attached trachea) will be transferred to EPL with the testes and epididymides and will be weighed at EPL, after removal of the trachea, and embedded in paraffin. The tissues will then** be sectioned at 3-5 microns and stained with hematoxylin and eosin (H and E) for subsequent histological evaluations. Optional tissues for histopathology include the liver, paired kidneys, adrenal glands (paired) and pituitary **(if warranted by organ weight** change of "significant magnitude"), **which will be placed in 10% neutral buffered formalin, and processed as above.** Stained sections will be evaluated by a Board Certified veterinary pathologist **(EPL)** for pathologic abnormalities and potential treatment-related effects. Thyroids should be evaluated for morphologic changes such as altered follicular epithelial height, the relative number and staining characteristics of colloid, the extent of thyroid vascular supply, and the density, size, and shape of the thyroid follicles. The one testis and epididymis per male will be evaluated for spermatogenesis, spermiogenesis, status of seminiferous tubules in the testis, and sperm in the epididymis, as well as the structural integrity of these organs."

Justification: Clarification of changes in histology and pathology procedures resulting from designating EPL as the histology laboratory (closing of RTI Histology Laboratory

effective 07/01/02; procedures for thyroid clarified through e-mail and telecon, J. George and J. Seely, 09/24/02; J. Kariya to D. Houchens, 11/01/02). Addition of the fixation medium for optional tissues, which was inadvertantly left out of the protocol.

Item 15

Section 7.0, Reporting, page 19, which reads:

"An executive summary will be prepared describing the number and strain of rats used in the study, the doses and chemicals tested, and the effects with levels of statistical significance for all endpoints. Electronic and hard copies of spreadsheets containing the raw data from all animals will be provided for each endpoint. In addition, the spreadsheet should include treatment means, standard deviation, standard error, coefficient of variation, and sample number below each endpoint. Data presented should include animal number and treatment, block and day of necropsy (if study conducted in blocks or animals killed on pnd 52 and 53), age and weight at preputial separation, body weights at weaning, organ and body weights at necropsy, body weight change from pnd 23 to necropsy, and serum T4 and TSH. A data summary table containing the mean, standard deviation, standard error, coefficient of variation, and sample size for each treatment group should be provided for all endpoints. Organ weights may be presented after covariance adjustment for necropsy body weight, but this should not replace presentation of the unadjusted data. Summaries of any histopathologic findings with photomicrographs of significant observations will also be provided."

is hereby amended to read:

7.0 Reporting

7.1 Status Reports

Status reports will be provided to the EDSP Program Manager.

7.2 Draft and Final Reports

A draft report will be submitted to the Sponsor's Representative within four months of the last necropsy date. The final report will include, but will not be limited to:

- Abstract
- Materials and Methods
- Results
- Discussion
- Conclusions
- References
- Summary in-life and necropsy data with statistical analyses
- Individual animal data: in-life and necropsy
- Protocol, any amendments, or any deviations from the protocol

Electronic and hard copies of ASCII files containing the raw data from all animals will be provided for each endpoint after final approval of the study report. A key will be provided identifying the type of data in each column of the ASCII file. In the report, summary data for F0 endpoints will be presented as combined data containing mean, standard deviation, and sample size. For F1 data, a data summary table containing the mean, standard deviation, standard error, coefficient of variation, and sample size for each treatment group should be provided for all endpoints. Organ weights may be presented after covariance adjustment for necropsy body weight, but this should not replace presentation of the unadjusted data. Summaries of any histopathologic findings with photomicrographs of significant observations will also be provided.

Summary of F0 Maternal Data

a. Survival indices

b. Gestational length

c. Mean litter size

d. Mean number of live and dead offspring

e. Number and percent of mothers showing treatment-related behavioral abnormalities in nesting and nursing (i.e., distocia, neglecting offspring, no milk visible in pups' stomach).

f. Gestational index (%) = $\frac{\text{No. pregnant females with live litters}}{\text{No. pregnant females}} \times 100$

Individual F0 Maternal Data

a. Identification number

b. Age at beginning of study

c. Age at death and manner of death

d. Gestational length in days

e. Total number of offspring per litter

f. Number and percent of live and dead offspring

g. General condition of offspring and mother through weaning

Summary of F1 Litter Lactational Data

a. Total litter size

b. Number and percent of stillborn

c. Number and percent of live births

d. Periodic viability counts

e. Periodic body weights by sex per litter from birth to weaning (taken on pnd 0, 4, 7, 14, and 21 by individual pup)

f. **Sex ratio (% males per litter)**

g. **Indices:**

Live birth index: = $\frac{No.\,live\,pups\,at\,birth}{Total\,no.\,pups\,born} x 100$

4-day survival index = $\frac{No.\,pups\,surviving\,4\,days\,(precull)}{Total\,no.\,live\,pups\,at\,birth} x 100$

7-day survival index = $\frac{No.\,pups\,surviving\,7\,days}{Total\,no.\,live\,pups\,at\,4\,days\,\,(postcull)} x 100$

14-day survival index = $\frac{No.\,pups\,surviving\,14\,days}{Total\,no.\,live\,pups\,at\,7\,days} x 100$

21-day survival index = $\frac{No.\,pups\,surviving\,21\,days}{Total\,no.\,live\,pups\,at\,14\,days} x 100$

Lactation index = $\frac{No.\,pups\,surviving\,21\,days}{Total\,no.\,live\,pups\,at\,4\,days\,(postcull)} x 100$

Individual Data From Retained F1 Male Offspring

a. **Identification number**

b. **Age at death and manner of death**

c. **Daily body and food weights from pnd 23 through pnd 52/53**

d. **Age and body weight at acquisition of preputial separation**

e. **Organ weights**

f. Reproductive system external and/or gross abnormalities

g. Histopathological observations

Summary of Data From Retained Male F1 Offspring

a. Mean periodic body weights and weight gains

b. Mean periodic feed consumption

c. Age and body weight at acquisition of preputial separation

d. Organ weights

e. Reproductive system external and/or gross abnormalities

f. Histopathological observations

Justification: Clarification of reporting procedures.

Item 16

Section 8.0, Personnel, page 20, which reads:

Study Director:	Julia D. George, Ph.D.
Project Toxicologist:	Rochelle W. Tyl, Ph.D., DABT
ARF Veterinarian:	Donald B. Feldman, D.V.M., ACLAM
ARF Manager:	Frank N. Ali, M.B.A., RLATG, ILAM
Laboratory Supervisor:	Melissa C. Marr, B.A., RLATG
Data Analyst and Reproductive Toxicity Supervisor:	Christina B. Myers, M.S.
Statistical Advisor:	Gayle. S. Bieler, M.S.

Research Data Entry Assistant:	Timothy W. Wiley, B.S.
Research Biologist:	William R. Ross, B.A.
Biologists:	Vickie I. Wilson
	Lawson B. Pelletier, RVMT, LAT
Biological Laboratory Assistants:	Marian V. Rieth, RVMT
	Malcolm D. Crews, ALAT
	Robin T. Krebs, ALAS
Endocrinology:	Patricia A. Fail, Ph.D.
	Carol S. Sloan, M.S.
	Kristi D. Vick, B.S.
Quality Assurance:	Doris J. Smith, B.S., Manager
	Celia D. Keller, M.S.
	Patricia D. Hall
	Marcia D. Phillips, M.S.
	D. Denise Rowe, M.L.S.
	Tiffany M. Kennedy, B.S.
	Erica D. Shinauld, B.S.
Histology:	Tsai-Ying Chang, B.S. HT-ASCP
Pathology:	John C. Seely, D.V.M., ACVP (EPL, Inc.)

Additional study team members to be determined.

is hereby amended to read:

Study Director:	Julia D. George, Ph.D.
Project Toxicologist:	Rochelle W. Tyl, Ph.D., DABT
ARF Veterinarian:	Donald B. Feldman, D.V.M., ACLAM
ARF Manager:	Frank N. Ali, M.B.A., RLATG, ILAM
Laboratory Supervisor:	Melissa C. Marr, B.A., RLATG

Data Analyst and Reproductive Toxicity Supervisor:	Christina B. Myers, M.S.
Statistical Advisor:	Gayle. S. Bieler, M.S.
Research Data Entry Assistant:	Timothy W. Wiley, B.S.
Research Biologist:	William **P.** Ross, B.A.
Biologists:	Vickie I. Wilson
	Lawson B. Pelletier, RVMT, LAT
Biological Laboratory Assistants:	Malcolm D. Crews, ALAT
	Robin T. Krebs, ALAT
Endocrinology:	Patricia A. Fail, Ph.D.
	Carol S. Sloan, M.S.
	Kristie D. Vick, B.S.
	Angela Parham, B.S.
Quality Assurance:	Doris J. Smith, B.S., Manager
	Celia D. Keller, M.S.
	Marcia D. Phillips, M.S.
	D. Denise Rowe, M.L.S.
	Tiffany M. **Kenney**, B.S.
	Erica D. **Shinuald**, B.S.
	Jennifer E. Jones, B.S.
	Jacques Hargett, B.S.
Histology:	**EPL, Incorporated**
Pathology:	John C. Seely, D.V.M., ACVP (EPL, Inc.)

Additional study team members to be determined.

Justification: Correction of typographical errors, inclusion of new study team members, deletion of personnel no longer working at RTI, designation of EPL as the histopathology laboratory.

Item 17

Note to the record:

Effective 6/10/02, Terri L. Pollock, B.A. was named Battelle Quality Assurance Manager for this project.

Marcia D. Phillips, M.S., the RTI International Quality Assurance Officer assigned to this contract will sign for the RTI QAU.

Justification: Designation of change in signatory Quality Assurance personnel.

APPROVED BY:

Rochelle W. Tyl, Ph.D., DABT Date
Project Toxicologist
Center for Life Sciences and Toxicology
Research Triangle Institute

Julia D. George, Ph.D. Date
Study Director
Center for Life Sciences and Toxicology
Research Triangle Institute

James P. Kariya Date
Work Assignment Manager
Endocrine Disruptor Screening Program U.S. EPA

David P. Houchens, Ph.D. Date
Program Manager
Endocrine Disruptor Screening Program
Battelle Memorial Institute

L. Greg Schweer Date
Project Officer
Endocrine Disruptor Screening Program U.S. EPA

REVIEWED BY:

Marcia D. Phillips, M.S. Date
Quality Assurance Specialist
RTI International

Terri L. Pollock, B.A. Date
Quality Assurance Manager
Battelle Memorial Institute

EPA Contract No. 68-W-01-023 (Battelle Prime Contractor)
RTI Contract No.: 65U-08055.001.015.001
RTI Master Protocol No.: RTI- 831
RTI Study Code: Rt02-ED03

Amendment 2 1/8/04

TITLE: Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 To 52/53

SPONSOR: Battelle Memorial Institute
505 King Avenue
Columbus, OH 43201-2693

TESTING FACILITY: RTI International
Chemistry and Life Sciences
Center for Life Sciences and Toxicology
Post Office Box 12194
Research Triangle Park, NC 27709

Study Protocol RTI-831, is hereby amended as indicated below (changes are **bolded** for clarity).

Item 1

Title page, page 1, protocol title, which reads:

"Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 Through 52/53"

is hereby amended to read:

"Assessment of Pubertal Development and Thyroid Function in Juvenile Male CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 23 **To** 52/53."

Justification: The animals were not to be dosed on the day of necropsy, i.e., pnd 52 or 53. Therefore, the correct terminology is "Postnatal Days 23 to 52/53 (effective 5/20/02)."

Item 2

Applicable sections of the protocol:

It is hereby noted that finasteride, one of the proposed test chemicals, was not, in fact, tested in the present study (E-mail communication from J. Kariya, EPA WAM, 10/10/02).

Section 3.4, Treatment of F1 Weanling Males, page 16, second sentence, which reads:

"Each animal will be weighed every other day prior to treatment and the body weight recorded."

Is hereby amended to read:

"Each animal will be weighed **every day** prior to treatment and the body weight recorded."

Justification: Correction of an error in the text. The animals were weighed daily.

Item 3

Section 3.4, Treatment of F1 Weanling Males, page 16, third sentence, which reads:

"Treatments will be administered daily by oral gavage in 5 ml corn oil/kg body weight from pnd 23 and continuing through pnd 52/53."

and

Section 3.5.1, Clinical Observations, page 16, first sentence, which reads:
"Clinical observations of F1 male study animals will be documented at least once daily on pnd 21 and 22 (prior to dosing period) and at least twice daily, at dosing and one to two hours postdosing, throughout the dosing period (pnd 23 through pnd 52 or 53)."

and

Section 3.5.2, F1 Weanling Male Body Weights, page 17, first sentence, which reads:

"All F1 males will be weighed in the morning on pnd 21 and 22, and every day in the morning during the dosing period on pnd 23 through pnd 52/53, for adjustment of dosing volume based on the most recent body weight."

Are hereby changed to indicate that the dosing period was pnd 23 **to** pnd 52/53.

Justification: The animals were not to be dosed on the day of necropsy, i.e., pnd 52 or 53. Therefore, the dosing period should be denoted as pnd 23 to pnd 52/53 (effective 5/20/03).

Item 4

Section 4.0, STATISTICAL ANALYSES, page 18, first paragraph, which begins:

"All data for a single chemical (two doses) and concurrent vehicle control group (weaning body weight, body weights and weight gains, age and weight at preputial separation, body and organ weights at necropsy, and serum hormones) will be analyzed using either parametric ANOVA under the standard assumptions or robust regression methods (Zeger and Liang, 1986; Royall, 1986; Huber, 1967) which do not assume homogeneity of variance or normality."

is hereby amended by inserting the following sentences directly after:

"Frequency data will be analyzed by Chi-Square Test for Independence for differences among treatment groups (Snedecor and Cochran, 1967) and by the Cochran-Armitage Test for Linear Trend on Proportions (Cochran, 1954; Armitage, 1955; Agresti et al., 1990). When Chi-Square reveals a significant ($p<0.05$) difference among groups, then a Fisher's Exact Probability Test, with appropriate adjustments for multiple comparisons, will be used for pairwise comparisons between each treatment group and the control group."

Justification: A description of the statistical analysis to be used for homogeneous frequency data was inadvertently omitted from the protocol (effective 5/20/02).

Item 6

Section 10.0, References, page 22 to 26, add the following citations:

Agresti, A., C.R. Mehta, and N.R. Patel (1990). Exact inference for contingency tables with ordered categories. *J. Amer. Statist. Assoc.* **85**, 453-458.

Armitage, P. (1955). Test for linear trends in proportions and frequencies. *Biometrics* **11**, 375-386.

Cochran, W. (1954). Some methods for strengthening the common X2 tests. *Biometrics* **10**, 417-451.

Snedecor, G.W., and W.G. Cochran (1967). Statistical Methods. Sixth Edition, Iowa State University Press, Ames, IA.

Justification: References accompanying the description of the statistical analysis to be used for homogeneous frequency data was inadvertently omitted from the protocol (effective 5/20/02).

Item 7

To the record

During the course of this study, more than one set of designating numbers was used to denote the individual treatment groups in the two components. This memo serves to correlate the treatment group designations used in the different records of the report.

Study Protocol, RTI-831, Amendment 1

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)
		COMPONENT 1	
1	Corn oil (vehicle	0	0.0
2	Atrazine	75	15.0
3		150	30.0
4	p,p'DDE	50	10.0
5		100	20.0
6	Vinclozolin	30	6.0
7		100	20.0
8	Methoxychlor	25	5.0
9		50	10.0
		COMPONENT 2	
10	Propylthiouracil	2	0.4
11		25	5.0
12	Ketoconazole	50	10.0
13		100	20.0
14	Linuron	50	10.0
15		100	20.0
16	Phenobarbital	50	10.0
17		100	20.0
18	Finasteride[b]	25	5.0
19		50	10.0
20	Corn oil (vehicle	0	0.0

[a] Finasteride was unavailable, and was not tested in this study.

Dose Code Form/Study Data Sheets

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)	5 digit Rx Code	Color Code
		COMPONENT 1			
1	Corn oil (vehicle control)	0	0.0	78967	Orange
2	Methoxychlor	25	5.0	96509	Blue
3		50	10.0	68843	Red
4	Atrazine	75	15.0	84156	Purple
5		150	30.0	39239	Brown
6	4,4' DDE	50	10.0	29505	Pink
7		100	20.0	48266	Yellow
8	Vinclozolin	30	6.0	15492	Green
9		100	20.0	07983	Black
		COMPONENT 2			
1	Corn oil (vehicle control)	0	0.0	82703	Purple
2	Propylthiouracil	2	0.4	04691	Pink
3		25	5.0	65437	Black
4	Linuron	50	10.0	46916	Green
5		100	20.0	59969	Yellow
6	Ketoconazole	50	10.0	27489	Red
7		100	20.0	16317	Blue
8	Phenobarbital	50	10.0	34563	Orange
9		100	20.0	95962	Brown

Battelle, Sequim Formulation ID Number

Chemical	Concentration (mg/ml)	Formulation ID Number
	COMPONENT 1	
Corn oil (vehicle control)	0	2-14-H-M
Vinclozolin	6	2-14-J-M
	20	2-14-K-M
Methoxyclor	5	2-14-L-M
	10	2-14-M-M
4,4' DDE	10	2-14-N-M
	20	2-14-P-M
Atrazine	15	2-14-Q-M
	30	2-14-R-M
	COMPONENT 2	
Corn oil (vehicle control)	0	2-14-A-M
Propylthiouracil	0.4	2-14-B-M
	5	2-14-C-M
Linuron	10	2-14-D-M
	20	2-14-E-M
Ketoconazole	10	2-14-F-M
	20	2-14-G-M
Phenobarbital	10	2-14-H-M
	20	2-14-I-M

Histopathology report (EPL, Inc.)

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)
		COMPONENT 1	
1	Corn oil (vehicle control)	0	0.0
2	Methoxychlor	25	5.0
3		50	10.0
4	Atrazine	75	15.0
5		150	30.0
6	p,p'DDE	50	10.0
7		100	20.0
8	Vinclozolin	30	6.0
9		100	20.0
		COMPONENT 2	
1	Corn oil (vehicle control)	0	0.0
2	Propylthiouracil	2	0.4
3		25	5.0
4	Linuron	50	10.0
5		100	20.0
6	Ketoconazole	50	10.0
7		100	20.0
8	Phenobarbital	50	10.0
9		100	20.0

Appendix I – Individual Animal Data Tables

Group No.	Chemical	Dose (mg/kg/day)	Concentration (mg/ml)
		COMPONENT 1	
1	Corn oil (vehicle control)	0	0.0
2	Atrazine	75	15.0
3		150	30.0
4	p,p'DDE	50	10.0
5		100	20.0
6	Vinclozolin	30	6.0
7		100	20.0
8	Methoxychlor	25	5.0
9		50	10.0
		COMPONENT 2	
10	Corn oil (vehicle control)	0	0.0
11	Propylthiouracil	2	0.4
12		25	5.0
13	Ketoconazole	50	10.0
14		100	20.0
15	Linuron	50	10.0
16		100	20.0
17	Phenobarbital	50	10.0
18		100	20.0

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