FINAL REPORT

ON

PUBERTAL ASSAYS IN AN ARRAY OF CHEMICALS: Assessment of Pubertal Development and Thyroid Function in Juvenile Female CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 22 to 42/43

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FINAL REPORT

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August 27, 2002 - October 10, 2002
(Component 1)

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(Component 2)

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September 18, 2002 (Component 1)
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FINAL REPORT

Assessment of Pubertal Development and Thyroid Function in Juvenile Female CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 22 to 42/43

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 female 20-day pubertal assay with thyroid assessment to evaluate test materials that are effective orally, or after a dosing duration longer than that used in the uterotrophic assay (EDSTAC Report, 1998). This assay is the most comprehensive in the proposed Tier 1 battery of assays. It can detect substances that alter thyroid function, are aromatase inhibitors, estrogens, anti-estrogens, and agents that interfere with the hypothalamus-pituitary-gonadal axis. Although 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 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 six additional chemicals that have various modes of action (i.e., atrazine, fenarimol, methoxychlor, bisphenol A, ketoconazole, and proplythiouracil), using the female pubertal assay.

The study was conducted in two components. In each component, F1 females, produced from undosed timed-pregnant CD® (Sprague-Dawley) rats (the F0 generation), were tested. On the day of birth [postnatal day (pnd 0)], F1 pups were counted, sexed, weighed, and examined externally. On pnd 4, the litters were standardized to 10 pups, maximizing the number of female 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 females were weaned and weight ranked across litters, then randomized into the treatment groups based on body weight. Fifteen F1 females were assigned to each treatment group in each component. F1 females were orally dosed with a test compound or the vehicle (Mazola® corn oil) from pnd 22 to pnd 42 or 43. Dose volume (5 ml/kg/day) was based on daily body weight. In Component 1, animals received atrazine (75 or 150 mg/kg/day), fenarimol (50 or 250 mg/kg/day), or methoxychlor (25 or 50 mg/kg/day) in corn oil. In Component 2, animals received bisphenol A (400 or 600 mg/kg/day), ketoconazole (50 or 100 mg/kg/day), or propylthiouracil (2 or 25 mg/kg/day) in corn oil. A separate vehicle control group dosed with corn oil was run concurrently with each component. Body weight and feed consumption for the F1 females were recorded during the

postweaning treatment period to scheduled sacrifice. Clinical signs were recorded twice daily during the treatment period. Beginning with pnd 22, F1 females were examined for vaginal patency. The day of complete vaginal patency was identified as the age of vaginal opening. Estrous cyclicity was monitored from the day of vaginal opening until necropsy.

At necropsy on pnd 42/43, females were euthanized and blood was collected by external cardiac puncture for analysis of thyroxine (T4) and thyroid-stimulating hormone (TSH). Body and selected organ weights were recorded, and a gross examination was conducted. The ovaries, uterus, and thyroid were evaluated histopathologically.

Observations

The following observations were made:

- Atrazine. Treatment with atrazine at 75 or 150 mg/kg/day delayed puberty, as evidenced by delayed vaginal opening. The mean postnatal day of vaginal opening exhibited a significant delay at the high dose (36.4 days vs. 32.9 days for the control group). Body weight and body weight gain were both decreased at both dose levels. The average postnatal day of first estrus and the start or end of the first cycle was also delayed at both dose levels, as expected, given that vaginal opening was delayed. There was no significant effect of treatment on cycle length or uterine weight, with or without fluid. No differences were noted in circulating T4 or TSH levels, and no treatment-related histopathological changes were observed in the thyroid, ovaries, or uterus. Altered age at vaginal opening, an indicator of disrupted pubertal development, and decreased body weight were observed in the absence of persistent weight gain changes or histopathology.

- Fenarimol. An increase in circulating TSH levels was observed at 50 and 250 mg/kg/day and as such, was the only target parameter to exhibit a significant effect at the low dose of fenarimol. Decreased circulating T4 levels were observed at the high dose. These effects on thyroid hormone levels were consistent with the observation of minimal follicular hypertrophy in 33% of the high-dose thyroids. Acquisition of vaginal opening was not affected by treatment with fenarimol. However, decreased time spent in proestrus, decreased body weight and body weight change, decreased feed consumption and decreased adjusted pituitary weight were all observed at the high dose. Adjusted liver weight was significantly increased at both doses of fenarimol. Thus, circulating TSH levels were affected at the low dose in the absence of other persistent

changes, whereas the high dose produced additional evidence of disrupted pubertal development.

- Methoxychlor. Accelerated vaginal opening was observed at both 25 and 50 mg/kg/day methoxychlor. Decreased adjusted ovary weight was observed at the high dose. There was no treatment effect on any other adjusted organ weights, circulating thyroid hormone levels, or histopathology.

- Bisphenol A. The mean postnatal day of vaginal opening was not affected by bisphenol A treatment at either 200 or 600 mg/kg/day. Mean body weight of the high-dose animals was significantly reduced on the day of acquisition, compared to the controls. Adjusted paired ovary weight exhibited a decreasing trend, accompanied by ovarian hypoplasia in 21% of the high dose animals. No other significant treatment-related changes were noted.

- Ketoconazole. The mean day of vaginal opening was not affected by ketoconazole treatment. Effects observed at the high dose included an increase in the average number of days spent in the first estrous cycle and a decrease in adjusted ovarian weight. In addition, ovarian pathology that increased in incidence and severity with dose, was observed at both 50 and 100 mg/kg/day. Cytoplasmic vacuolization of the corpora lutea was observed in 12/15 and 9/15 of the low and high-dose animals, respectively. The five remaining animals in the high-dose group exhibited a complete absence of corpora lutea.

- Propylthiouracil. As expected, propylthiouracil produced a decrease in circulating T4 levels, and an increase in circulating TSH levels, increased adjusted thyroid weight, and thyroid follicular cell hypertrophy/hyperplasia at both 2 and 25 mg/kg/day. There was no significant effect of treatment on acquistion of vaginal opening, or any other parameter of female pubertal development. In addition, other than the thyroid, treatment with propylthiouracil did not affect adjusted organ weights.

OBJECTIVE

The objective of this study was to examine the sensitivity of the female pubertal assay to the effects of many chemicals known to affect the endocrine system through different pathways and/or mechanisms of action. This is the most comprehensive assay in the proposed Tier 1

battery of assays. It is capable of detecting substances that alter thyroid function that are aromatase inhibitors, estrogens, antiestrogens, and that are agents that interfere with the hypothalamus-pituitary-gonadal and/or hypothalamus-thyroid axis. Results from other shorter assays and/or with the use of intraperitoneal (ip) injection as the route of administration, have also been reported (O'Connor et al., 1999a, b; 2000; 2002a, b). Although 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 six additional chemicals that have various modes of action.

MATERIALS AND METHODS

Test Materials and Dose Formulations

The test chemicals used in this study were procured and analyzed for purity by the Sponsor, as indicated below by gas chromotography with flame ionization detection (GC-FID), high pressure liquid chromotography (HPLC), or gravimetric methods. All bulk test chemicals were stored at room temperature.

Atrazine

CAS Number:	1912-24-9
Supplier:	Chem Services
Lot. No.:	285-63B
	289-102A
Purity (Battelle):	98% (GC-FID)
	98% (GC-FID)

Fenarimol

CAS Number:	60168-88-9
Supplier:	Chem Services
Lot. No.:	287-5B
Purity (Battelle):	99.7% (GC-FID)

Methoxychlor

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

Bisphenol A

CAS Number:	80-05-7
Supplier:	Fisher
Lot. No.;	A0147444
Purity (Battelle):	100.0% (HPLC)

Ketoconazole

CAS Number:	65277-42-1
Supplier:	Spectrum Laboratory Products
Lot. No:	QL0352
Purity (Battelle):	100.0% (HPLC)

Propylthiouracil

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

Mazola® corn oil was purchased by Battelle-Sequim from retail outlets. Peroxide determination of the corn oil 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). Thus, all corn oil purchased for this study was verified to have a peroxide number less than 3 meq/kg. 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, 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 8 weeks, with the exception of fenarimol, which was stable for 6 weeks, and methoxychlor, which was stable for 4.5 weeks. Formulations assayed (triplicate average) between 90.5% and 112% of the target concentration prior to shipping to RTI International (Tables 1-A through 1-F). 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 August 19, 2002 at gestational day (gd) 13 (Table 1). A separate order of 20 timed-pregnant and 2 nonpregnant female rats were received on October 28, 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, Fenarimol, Methoxychlor)	
Receive 20 females at gd 13	August 19, 2002
Quarantine (gd 13-20)	August 19–25, 2002
pnd 0	August 27-28, 2002
pnd 21	September 17-18, 2002
1st day of dosing (pnd 22)	September 18-19, 2002
Necropsy (pnd 43)	October 8-10, 2002
Component 2 (Bisphenol A, Ketoconazole, Propylthiouracil)	
Receive 20 females at gd 13	October 28, 2002
Quarantine (gd 13-20)	October 28–November 4, 2002
pnd 0	November 5-6, 2002
pnd 21	November 26-27, 2002
1st day of dosing (pnd 22)	November 27-28, 2002
Necropsy (pnd 42)	December 17-19, 2002
Reproductive organ/thyroid histopathology report	October 28, 2003
Hormone sample analysis	March 19, 2003

For each component, the animals were quarantined for 1 week, during which time they were examined by a veterinarian. Representative animals were subjected to fecal examination.

Within 1 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 pulmon26is*, (*M. Pul.*) and
- parvo (PARVO).

Results of the physical examination, serology, and parasitology were negative for signs of infectious disease. The animals were considered 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 during lactation in solid-bottom polycarbonate cages with stainless-steel wire lids (Laboratory Products, Rochelle Park, NJ) and Sani-Chip® cage litter (P.J. Murphy Forest Products Inc., Montville, NJ). Postwean, retained F1 females were housed singly until necropsy. All animals were housed in the RTI Animal Research Facility for the duration of the study. 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). No light cycle deviations occurred during either component of the study. The protocol-mandated temperature range was 64-79°F (18-26°C), and the RH range was 30-70% (NRC, 1996). The F0 and F1 animals in Component 1 were housed in Room 204 of the Animal Research Facility. Temperature and RH readings for the animal rooms, excluding transient deviations, which are presented in the Protocol Deviation list (page 38), are presented here. Temperature and RH readings for Room 204 from August 19 to October 10, 2002, were 69.2 to 73.5°F and 43.4 to 60.2% RH. F0 and F1 animals in Component 2 were housed in room 204 from October 28 to November 25, 2002. Due to a malfunction in the environmental control system in the Animal Research Facility that affected the humidity in Room 204, animals in Component 2 (F0 females and preweanlings) were transferred to Room 202 on the afternoon of November 25, 2002, where they remained until necropsy. Temperature and RH readings for Room 204 from October 28 to November 25, 2002 were 70.5 to 73.2°F and 48.2 to 62.8% RH.

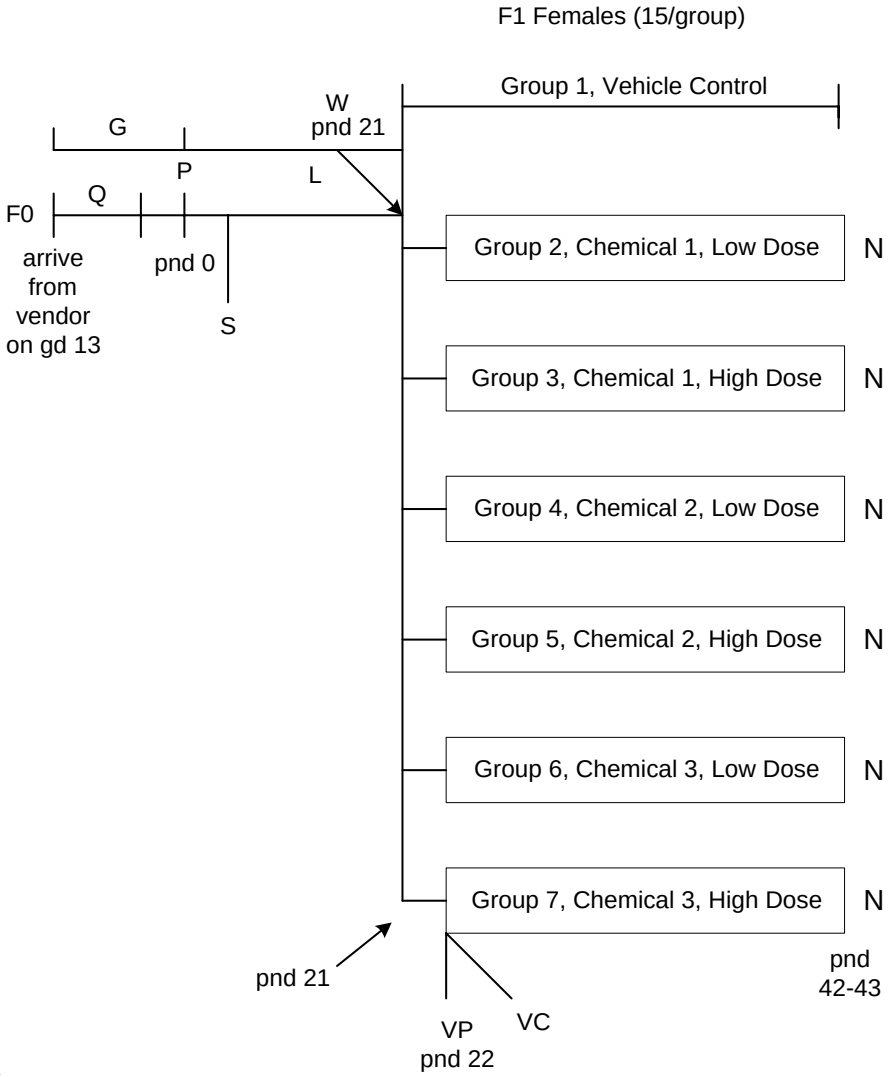
Temperature and RH readings for Room 202 from November 25 to December 19, 2002 were 70.5 to 73.8°F and 39.0 to 69.3% RH.

Purina Certified Rodent Chow (No. 5002, PMI Feeds, Inc., St. Louis, MO; batch number documented in the study records) was available *ad libitum*. All animals in all groups received the same batch/lot (lot #JUN 24 02 1B) of Purina Certified Rodent Chow at all times. The analysis of the feed batch for nutrient levels and possible contaminants was performed by the manufacturer, examined by the Study Director, and maintained in the study records. The mean metabolizable energy value (kcal/gm) for feed milled in 2002 was 3.10 kcal/gm (Appendix IV). The feed was also analyzed by the manufacturer for the phytoestrogens daidzein, genistein, and glycitein. Triplicate analysis (samples 1, 2, and 3) of lot #JUN24021B indicated that the total phytoestrogen aglycones in this lot of feed ranged from 341 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. (Freemont, 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 ten pups, maximizing the number of female pups. A total of 15 F1 females per group was assigned to each component in this study. F1 females 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 female F1 weanlings were identified by eartag; F1 pups were not uniquely identified prior to weaning. The method and numbers for identification were documented in the study records. After selection of the F1 female weanling study animals, four unselected female 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 while 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 females, the sentinels were terminated, blood samples collected, and serum samples prepared. All sentinel serum samples were submitted to BioReliance (Rockville, MD) for serological evaluations (see above). Analysis of serum (as described above) from sentinels sacrificed during the necropsy of the retained F1 female necropsy was negative for viral antibodies.

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 used in the study, were removed from the study room when the F0 females were released from quarantine and euthanized. Similarly, F1 females not assigned to treatment groups or chosen as sentinels were euthanized. Records were kept documenting the fate of all animals in the study.



KEY:

_____ No test chemical exposures to F0 dams or F1 offspring during gestation or lactation. F1 females in Group 2 dosed with corn oil.

▭ Direct once daily gavage dosing with test chemical of F1 females starting on pnd 22 (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

S = Standardize litters to ten with maximum number of F1 female pups (discard culled pups)

VP = Acquisition of vaginal patency (evaluation began on pnd 22)

VC = Vaginal cytology (evaluation began on the day of VP)

N = Necropsy (see text)

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

Study Design

A graphic representation of the component study design is presented in Figure 1. The study began with 20 timed-mated F0 females in each component.

F0 Females

Beginning on gestational day (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. 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 that 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 female 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 Females

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

Beginning on pnd 22, each F1 female was dosed with a test material at one of the selected dose levels or the vehicle control (corn oil for all chemicals), as shown in Table 2. EPA selected the seven 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, fadrazole, an aromatase inhibitor that interferes with conversion of testosterone to 17β-estradiol in both sexes, could not be obtained from the manufacturer in time to be included in the study, and was eliminated from current testing. The remaining six test chemicals and their target/mechanism of action are as follows:

1. atrazine (affects the hypothalamus-pituitary axis in female rats and ovulation);

2. fenarimol (a weak aromatase inhibitor);

3. methoxychlor (a xeno-estrogen through α-estrogen receptor, anti-estrogen through β-estrogen receptor and an anti-androgen through androgen receptor mediated mechanism);

4. bisphenol A (a weak environmental estrogen which binds to both the α and β estrogen receptor);

5. ketoconazole (inhibits steroidogenesis in both sexes); and

6. propylthiouracil (affects the thyroid directly, causing hypothyroidism).

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

Group No.	No. F1 Females	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	Fenarimol	50	10.0	5
5	15		250	50.0	5
6	15	Methoxychlor	25	5.0	5
7	15		50	10.0	5
COMPONENT 2					
1	15	–[a]	0	0.0	5
2	15	Bisphenol A	400	80.0	5
3	15		600	120.0	5
4	15	Ketoconazole	50	10.0	5
5	15		100	20.0	5
6	15	Propylthiouracil	2	0.4	5
7	15		25	5.0	5

[a] Corn oil, vehicle control

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 22 and continuing to pnd 42/43. This duration of treatment was unnecessary to detect estrogenic chemicals but was required for the detection of pubertal delay and antithyroid effects. Test chemicals were administered in corn oil vehicles 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 female study animals were documented at least once daily on pnd 21 (prior to dosing period) and at least twice daily, at dosing and one to two hours postdosing, throughout the dosing period (pnd 22 to pnd 42 or 43). All F1 females were weighed in the morning on pnd 21 and every morning during the dosing period on pnd 22 to pnd 42/43, for adjustment of dosing volume based on the most recent body weight. Daily body weights were reported and statistically analyzed. F1 female weight gains were calculated and analyzed for pnd 21-22, 22-28, 28-34, 34-40, 40-42, 42-43, and 22-42/43 (treatment period). F1 female body weights were also recorded on the day of acquisition of vaginal patency. Feed consumption for the individually-housed F1 weanling females was recorded daily and reported as g/day and as g/kg body weight/day.

Beginning on pnd 22, each F1 study female was examined daily for vaginal patency. The appearance of a small "pin hole," a vaginal thread, as well as complete vaginal opening was recorded on the days they were observed. The day of complete vaginal patency was the endpoint used in the analysis for the age of vaginal opening. Body weight at acquisition of complete vaginal patency was recorded.

Beginning on the day of vaginal opening and continuing until pnd 42/43, daily vaginal smears were obtained from each F1 female and evaluated to determine the age at first estrus, age at the first complete vaginal cycle, and/or any effects on estrous cyclicity. The number of animals in each treatment group that went through at least one complete cycle, and the number of days each animal spent in each stage of the estrous cycle was calculated. Analysis based both on pnd and by day-since-vaginal-patency was conducted for the onset of estrus. Indicators of estrous cyclicity were compared between control and treated groups.

Necropsy for pnd 42/43 F1 Females

Blood Collection and Hormone Assays. At scheduled necropsy of the F1 females, after terminal anesthesia (CO_2 asphyxiation), the females 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 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).

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 phosphate buffered saline 1% [w/v] bovine serum albumin, and 0.1% (w/v) sodium azide, pH 7.6). T4 controls were prepared in the same matrix as unknown samples by adding known concentrations of T4 to pubertal female serum. 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

Parameter	Hormone Assay	
	T4 (µg/dL)	rTSH (ng/ml)
Matrix	pubertal female serum	pubertal female serum
Intra-assay Variation:[a]		
blank matrix	0/5.7%	0/10.5%
mass added	2/3.5% 10/2.9%	8/5.1% 32/3.6%
Interassay Variation:[a]		
number of assays	3	2
blank matrix	0/7.4%	0/4.5%
mass added	2/8.6% 10/6.1%	8/9.0% 32/8.9%
% Recovery of Added Mass[b]	2/(63.0% - 88.0%) 10/ (78.4% - 87.5%)	8/(89.6%- 114.8%) 32/(98.0% - 116.1%)
Index of Parallelism[c]	2/99.7%[d] 10/104.4%[d]	0/120.3% 8/100.4% 32/101.1%

[a] Numbers are the concentration of the mass added/percentage variations. For intra-assay variation, the number of samples assayed was ten in each case.
[b] Numbers are the concentration of the 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 female 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: liver, kidneys (paired), adrenal glands (paired), ovaries (paired), uterus, thyroid (with attached portions of trachea), and pituitary. For the uterine dissection, care was taken to remove mesenteric fat from the uterine horns and not damage the uterus so that the uterine fluid was retained. The uterus (without ovaries) was carefully dissected and trimmed of fascia and fat to avoid loss of luminal contents. The vagina was removed from the uterus at the level of the uterine cervix.

Tissues taken at necropsy were placed in fixative and then transferred to Experimental Pathology Laboratories (EPL) for processing. In Component 1, the ovaries, uterus, and thyroid with attached portions of trachea 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 was weighed at EPL, after removal of the trachea. The tissues were sectioned at 3-5 microns and stained with hematoxylin and eosin (H and E) for subsequent histological evaluations. Pathologic evaluation

of the thyroid revealed that fixation in Bouin's fixative rendered the tissue too dark and too brittle for optimal evaluation. The thyroids from animals in Component 2 were fixed in 10% neutral buffered formalin. No optional tissues were evaluated, but have been retained in 10% neutral buffered formalin for optional histopathology. Stained sections were evaluated for pathologic abnormalities and potential treatment-related effects by an AVCP board-certified veterinary pathologist.

Statistical Analyses

All data for a single chemical (two doses) and a 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). When 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. When 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 the 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 female offspring on study.

Frequency data were 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 revealed a significant ($p<0.05$) difference among groups, then a Fisher's Exact Probability Test, with appropriate adjustments for multiple comparisons, was used for pairwise comparisons between each treatment group and the control group.

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 female body and organ weights. When 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. J. D. George served as Study Director. Reproductive and Developmental Toxicology personnel included Ms. M.C. Marr (Laboratory Supervisor), Ms. C.B. Myers (Reproductive Toxicity Study 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 Feeds, Inc., and included as Appendix IV. The protocol and two amendments, detailing the design and conduct of the study is presented in Appendix V of this report. Protocol deviations are listed on page 38, 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 Chemistry and Life Sciences Archivist, and remains 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 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. 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 90.5-112% of the target concentrations and were homogeneous (Table 1-A to 1-F). Aliquots of the dosing solutions and the control formulations were taken on the first day of dosing (the first pnd 22) and on the first pnd 28, 35, and 42. For Component 1, pnd days 22, 28, 35, and 42 corresponded to September 18 and 24, 2002, and October 1 and 8, 2002, respectively. In addition, the dosing formulation remaining in the dosing jar after completion of dosing served as the postdosing analytical sample (Jar samples). For Component 2, pnd 22, 38, 35, and 42 corresponded to November 27, 2002, and

December 3, 10, and 17, 2002, respectively. In addition, the formulation remaining in the dosing jar was submitted for analysis (designated as Remain or Remainder samples; see Tables 1-A to 1-F and Chemistry Reports in Appendix III)).

Analysis of 15 mg/ml atrazine dose formulations indicated concentrations of 110–113% of the target concentration for the in-life samples, and 93% of the target concentration for the postdosing sample (Table 1-A). The 30 mg/ml atrazine formulation assayed at 107–110% for the in-life samples and 93% for the postdosing sample. Analysis of 10 mg/ml fenarimol dose formulations indicated concentrations of 109-116% of the target concentration for the in-life samples and 100% of the target concentration for the postdosing sample (Table 1-B). The 50 mg/ml fenarimol formulation assayed at 99.8–111% for the in-life samples and 102% for the postdosing sample. Analysis of the 5 mg/ml methoxychlor formulations indicated 92–99% of the target concentration for the in-life samples and 92–99% for the postdosing samples (Table 1-C). The 10 mg/ml methoxychlor formulation assayed at 90-94% for the in-life samples and 93% for the postdosing samples.

Analysis of 80 mg/ml bisphenol A dose formulations indicated concentrations of 99-109% of the target concentration for the in-life samples and 100% of the target concentration for the postdosing sample (Table 1-D). The 120 mg/ml bisphenol A formulation assayed at 104-112% for the in-life samples and 99% for the postdosing sample.

Analysis of 10 mg/ml ketoconazole dose formulations indicated concentrations of 81–109% of the target concentration for the in-life samples and 112% of the target concentration for the postdosing sample (Table 1-E). The 20 mg/ml ketoconazole formulation assayed at 96–103% for the in-life samples taken on pnd 22, 28, and 35 and 58% for the sample taken on pnd 42. The reason for the exceptionally low concentration of the pnd 42 sample is unknown. However, the postdosing sample, taken from the remainder of the dosing solution in the jar assayed at 110%.

Analysis of 0.4 mg/ml propylthiouracil dose formulations indicated concentrations of 86-97% of the target concentration for the in-life samples and 98% of the target concentration for the postdosing sample (Table 1-F). The 5 mg/ml propylthiouracil formulation assayed at 74-99% for the in-life samples, and 94% for the postdosing sample.

Additional analytical data are presented in Appendix III.

Component 1

Control F1 Females

Fifteen untreated F1 females 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, fenarimol, and methoxychlor. All fifteen control animals were evaluated at scheduled necropsy on pnd 42 or 43 (see below).

In-Life Data From F1 Females Treated With Atrazine

Fifteen untreated F1 females were assigned to the 0, 75, or 150 mg/kg/day atrazine group (Table 2-A). No animals assigned to the control group or either atrazine-treated group died prior to scheduled necropsy. Body weights at weaning (pnd 21) and on the day of initiation of dosing (pnd 22) were equivalent across treatment groups (Table 3-A). Daily body weights for F1 females were significantly decreased in the high-dose group compared to the control group from pnd 23 to scheduled necropsy on pnd 42 or 43. In the low dose group, body weight was decreased compared to the control group on pnd 31, 33, 34, 35, 37, 38, 39, 40, 41, and 42, but not prior to pnd 31, or on pnd 32, 36, or 43. Body weight change was equivalent across treatment groups for pnd 21 to 22, and was not affected by treatment with atrazine for 34 to 40, 40 to 42, or 42 to 43. However, body weight change was significantly less in both atrazine-treated groups compared to the control group for pnd 22 to 28, and for pnd 22 to 42, and in the high dose group only for pnd 28 to 34 and pnd 22 to 43 (Table 3-A).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) was equivalent across treatment groups (Table 4-A). The low and high dose atrazine-treated groups exhibited a significant dose-related decrease in absolute feed consumption on pnd 22-23 (15.9% and 38.6%, respectively), which was most likely influenced by the initiation of gavage dosing with the test compound, and subsequent aversion to the compound smell and/or taste. Thereafter, only the high dose group exhibited an effect on absolute feed consumption, with decreases (range of 33.3% to 10.5%) for pnd 23 to 24, 24 to 25, 25 to 26, 27 to 28, and 32 to 33, with the greater effect occurring during the first days of dosing. A significant decreasing trend was observed for only pnd 26 to 27, 28 to 29, 29 to 30, 34 to 35, and for the treatment period for animals necropsied on pnd 42 (pnd 22 to 42). When feed consumption was calculated as a percent of body weight (g/kg/day), feed consumption again exhibited a dose-related decrease for pnd 22 to 23, with both atrazine-treated groups affected (15.8% and 35.7%, low and high dose, respectively), and a decrease at the high dose on pnd 23 to 24 and 24 to 25 (24.8% and 12.4%, respectively). Thereafter, relative feed consumption tends to level out across the treatment groups, with a significant increase in relative feed consumption observed on pnd 30 to 31 and

pnd 38 to 39 (both atrazine-treated groups increased), and pnd 36 to 37 (high dose only). An increasing trend, only, was observed on pnd 37 to 38 and pnd 39 to 40. Relative feed consumption was equivalent across treatment group when calculated for the whole treatment period (pnd 22 to 42 or 22 to 43; Table 4-A).

Clinical observations were noted in the atrazine-treated groups and included rooting postdosing, salivation prior to dosing, and sore(s) in 4, 9, and 1 animal(s) in the high-dose group, respectively, and the same observations in 1, 6, and 1 animal(s) in the low-dose group, respectively (Table 5-A).

Treatment with atrazine resulted in a dose-related delay in vaginal opening, which was significant at the high dose (36.4 days vs. 32.9 days for the control group; Table 6-A). In addition, the average postnatal day of first estrus exhibited a dose-related delay that was significant at high dose compared to the control group (37.4 vs. 34.1). The same pattern was observed for the average postnatal day of the end of the first cycle. The average postnatal day of the start of the first cycle was significantly delayed at both doses. There was no significant effect of treatment on the average body weight on the day of acquisition of vaginal opening, although body weights tended to increase with dose, due to the delay in the acquisition of this landmark. In addition, there was no effect of treatment on the average number of days from vaginal opening until first estrus, the number or percent of females cycling, the average number of days from vaginal opening to the start or end of the first cycle, or the number of days spent in estrus, metestrus, or proestrus. The low-dose group, but not the high dose group, exhibited a significant shorter diestrus period compared to the control group. It is noteworthy that due to the delay in vaginal opening and subsequent first estrus, four of the high-dose animals could not be evaluated for estrous cyclicity, since there were not enough observation days after first estrus and prior to scheduled necropsy to collect an adequate number of smears. In addition, one female in the high-dose group was acyclic, although she exhibited vaginal opening and first estrus. It is not known whether this female would have exhibited estrous cycling if the observation period had been extended beyond pnd 42/43 (Table 6-A).

Necropsy and Histopathological Data from F1 Females 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 pituitary weight was decreased at the high dose, as was paired ovary weight, whereas liver weight exhibited a dose-related decreasing trend without significant pairwise comparisons. When organ weights were adjusted with respect to necropsy body weight, adjusted liver weight increased in a dose-related manner that was significant at both doses of atrazine. In addition, adjusted paired kidney weight exhibited an increasing trend, with the high-dose value

significantly greater than the control group value. Atrazine treatment had no significant effect on thyroid, adrenal, or uterine weights (with or without fluid), or on circulating T4 or TSH levels (Table 7-A).

Gross necropsy findings were minimal, and included one animal each in the control- and high-dose group with hydronephrosis, one animal in the high-dose group with a uterine cyst, and one animal each in the control and low-dose group with fluid in the uterus (Table 8-A). No treatment-related histopathology was observed (Appendix II).

In-Life Data from F1 Females Treated with Fenarimol

Fifteen untreated F1 females were assigned to each of the 0, 50, or 250 mg/kg/day fenarimol groups (Table 2-B). No animals assigned to the control group or either fenarimol-treated group died prior to scheduled necropsy. Body weight at weaning (pnd 21) and on the day of initiation of dosing (pnd 22) was equivalent across treatment groups (Table 3-B). Daily body weights for F1 females were significantly decreased in the high-dose group compared to the control group from pnd 23 to scheduled necropsy on pnd 42, but not on pnd 43. No significant effect on daily body weight was observed for the low-dose group. Body weight change was equivalent across treatment groups prior to initiation of treatment (pnd 21 to 22) and was not affected by treatment with fenarimol for pnd 34 to 40, 42 to 43, or 22 to 43. In the high-dose group, body weight was transiently increased on pnd 40 to 42. However, body weight change was significantly less in the high dose fenarimol-treated group compared to the control group for pnd 22 to 28, 28 to 34, and 22 to 42 (Table 3-B).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) exhibited an increasing trend, but there were no significant pairwise differences from the control group (Table 4-B). The high-dose fenarimol-treated group exhibited a significant decrease in absolute feed consumption (range of 60.6% to 26.3%) on pnd 22-23, 23 to 24, 24 to 25, and 25 to 26. The high-dose animals also consumed less feed (g/day) for the periods of pnd 29 to 30, 32 to 33, and 35 to 36. Absolute feed consumption was significantly reduced in the high-dose group for the treatment period measured from pnd 22 to 42 (10.7%) but not for pnd 22 to 43 (5.3% decrease compared to the control group). A significant decreasing trend, only, was observed for pnd 27 to 28, 31 to 32, and 33 to 34. When feed consumption was calculated as a percent of body weight (g/kg/day), a dose-related increasing trend was noted for pnd 21 to 22 (prior to initiation of treatment), while a significant decrease was noted in the high-dose group compared to the control group for pnd 22 to 23, 23 to 24 and 24 to 25. A significant <u>increase</u> in relative feed consumption was observed for the high-dose group for pnd 26 to 27, 27 to 28, 28 to 29, 30 to 31, 33 to 34, 34 to 35, 36 to 37, 37 to 38, 38 to 39, 39 to 40, 40 to 41, 22 to 42, and 22 to 43. In

addition, relative feed consumption was significantly increased at the low dose of fenarimol for pnd 25 to 26 and 30 to 31 (Table 4-B).

Clinical observations were noted in the fenarimol-treated groups and included rooting postdosing, salivation prior to dosing, and sore(s) in 5, 7, and 2 animal(s) in the high-dose group, respectively, and rooting postdosing and salivation prior to dosing in 6 and 4 animal(s) in the low-dose group, respectively (Table 5-B).

Treatment with fenarimol did not alter the average postnatal day of vaginal opening (Table 6-B). However, average body weight on the day of acquisition was significantly decreased at the high dose. There was no significant effect of treatment on the average number of days from vaginal opening until first estrus, the average postnatal day of first estrus, the number or percent of females cycling, the average number of days from vaginal opening to the end of the first cycle, or the number of days spent in diestrus, estrus, or metestrus during the first cycle. The average number of days from vaginal opening until the start of the first cycle was increased at the mid dose, but not at the high dose. The high dose exhibited a significant decrease in the number of days spent in proestrus during the first cycle (0.6 vs. 1.0 for the control group). Prolonged estrus was observed in 2/13 (15.4%) of the high-dose animals, compared to none in the control or low-dose fenarimol groups. Two of the high-dose animals could not be evaluated for estrous cyclicity, since there were not enough days after first estrus prior to scheduled necropsy to collect an adequate number of smears. In addition, two females in the low-dose group were acyclic, although they exhibited vaginal opening and first estrus. It is not known whether these females would have exhibited estrous cycling if the observation period had been extended beyond pnd 42/43 (Table 6-B).

Necropsy and Histopathological Data from F1 Females Treated with Fenarimol

At necropsy, average body weight was significantly decreased at the high dose of fenarimol compared to the control group (Table 7-B). Absolute pituitary weight was decreased at the high dose, as was the uterine weight (without fluid), whereas liver weight exhibited a dose-related increasing trend with a significant increase at the high dose. Paired kidney and paired ovary weights exhibited a decreasing trend. When organ weights were adjusted with respect to necropsy body weight, pituitary weight at the high dose was still significantly decreased compared to the control group, whereas liver weight increased in a dose-related manner that was significant at both doses of fenarimol. In addition, adjusted paired ovary weight and uterine weight without fluid exhibited a decreasing trend. Fenarimol treatment had no significant effect on thyroid or paired adrenal gland weights. Adjusted paired kidney weights exhibited a slight increase at both doses of fenarimol that was statistically significant at the low, but not the high dose. T4 levels were significantly decreased at the high dose (by 16% compared to the control

value), whereas circulating TSH levels exhibited a dose-related increase that was significant at both doses of fenarimol. The low- and high-dose fenarimol-treated groups exhibited a 30.2% and 104.3% increase, respectively, in the level of circulating TSH compared to the control group value (Table 7-B).

Gross necropsy findings were minimal and included one animal in each group with hydronephrosis, one animal in the high dose group with a shortened right uterine horn, one animal in the low-dose group with uterine cysts, and one to four animals in each group with a fluid filled uterus (Table 8-B). Minimal follicular hypertrophy of the thyroid was observed in 5/15 of the high dose females (Appendix II). As noted above, there was no significant effect of treatment on the absolute thyroid weight or in thyroid weight adjusted for either necropsy or pnd 21 body weight. However, circulating levels of T4 were significantly decreased, and TSH levels significantly increased at the high dose.

In-Life Data from F1 Females Treated with Methoxychlor

Fifteen untreated F1 females were assigned to the 0, 25, or 50 mg/kg/day methoxyclor groups (Table 2-C). One animal in the 25 mg/kg/day methoxychlor-treated group was found dead on pnd 38 prior to scheduled necropsy. Thus, 15, 14, and 15 animals in the control, low, and high dose groups were available for full evaluation in this study. Body weight at weaning (pnd 21) and on the day of initiation of dosing (pnd 22) was equivalent across treatment groups (Table 3-C). In addition, daily body weights for F1 females were unaffected by methoxychlor treatment through pnd 34. From pnd 35 through necropsy on pnd 42 or 43, body weight exhibited a decreasing trend, with a significant effect at the high dose for all time points from pnd 36 to 42. No significant effect on daily body weight was observed at the low dose of methoxychlor. Body weight change was equivalent across treatment groups for pnd 21 to 22 and was not affected by treatment with methoxychlor for 22 to 28, or 40 to 42. However, body weight change was significantly less in both methoxychlor-treated groups compared to the control group for pnd 28 to 34, 42 to 43, and 22 to 42, and also in the high dose group for pnd 34 to 40 and 22 to 43 (Table 3-C).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) and for the measured periods up to pnd 33, and pnd 33 to 34, 34 to 35, 37 to 38, 38 to 39, 39 to 40, 22 to 42, and 22 to 43 were equivalent across treatment groups (Table 4-C). Feed consumption was significantly depressed in both methoxychlor-treated groups for pnd 32 to 33, 40 to 41, 41 to 42, and 42 to 43. The decrease in feed consumption was similar for both treatment groups for any one time interval, and ranged from 9.0% to 26.5%, with the greater effects occurring in the late treatment period. Absolute feed consumption was decreased in the high dose group only on pnd 35 to 36, and 36 to 37 (approximately 11%). When feed consumption was calculated as a

percent of body weight (g/kg/day), a significant increase was noted in the high dose group compared to the control group for pnd 23 to 24, and 25 to 26. A decreasing trend was noted for pnd 32 to 33, 35 to 36, and 42 to 43, with values for both methoxychlor-treated groups significantly less than the control group value for pnd 42 to 43. Relative feed consumption was equivalent across treatment groups when calculated for the whole treatment period (pnd 22 to 42 or 43; Table 4-C).

Clinical observations were noted in the methoxychlor-treated groups and consisted of one animal in the high-dose group with rooting postdosing, and salivation prior to dosing in one and three animal(s) in the low and high-dose groups, respectively (Table 5-C). As noted previously, one animal was found dead during the postwean treatment period (Table 5-C).

Treatment with methoxychlor resulted in a dose-related acceleration in vaginal opening that was significant in both treated groups (Table 6-C). The average postnatal day of vaginal opening was 29.8 and 27.4 for the low- and high-dose groups, respectively, compared to 32.9 days for the control group. Body weight on the day of acquisition of vaginal opening was significantly depressed for both the low and the high dose methoxychlor-treated groups, secondary to the younger age of these animals at acquisition. The average postnatal day of first estrus exhibited a dose-related acceleration that was significant at both doses of methoxychlor (30.4 and 28.3 days for the low and high dose, respectively, compared to 34.1 days for the control group). All but one female in the low-dose group were observed to cycle. The average number of days from vaginal opening to the start of the first cycle exhibited a significant increasing trend (1.4-1.5 days vs. 0.1 days for the controls). A similar, although less distinct, and nonsignificant pattern was observed for the number of days from vaginal opening to the end of the first cycle. However, the average postnatal day of the start or end of the first cycle decreased in a dose-related manner, and the animals in the high-dose group were significantly younger than the control animals. The average number of days spent in diestrus or metestrus during the first cycle exhibited a slight decreasing trend. The percent of females exhibiting prolonged estrus was significantly increased at both dose levels of methoxychlor, and was 0, 46.7, and 33.3% in the control, low, and high-dose groups, respectively (Table 6-C).

Necropsy and Histopathological Data from F1 Females Treated with Methoxychlor

At necropsy, average body weight exhibited a dose-related decreasing trend, with the high-dose methoxychlor-treated group significantly below the control group (Table 7-C). Absolute paired ovary weight exhibited a decreasing trend, but no other significant treatment-related effects were observed for absolute organ weights. When organ weights were adjusted with respect to necropsy body weight, adjusted paired ovary weight still exhibited a decreasing trend. The paired ovary weights from the high-dose animals were significantly less than the

controls only for necropsy weight-adjusted values. Methoxychlor treatment had no other significant effects on adjusted organ weights, or on circulating T4 or TSH levels (Table 7-C).

Gross necropsy findings were minimal, and included one animal in each group with hydronephrosis, and one to six animals in each treatment group with a fluid-filled uterus (Table 8-C). Minimal hyperplasia of the uterine epithelium was observed in 5/15 of the high dose females (Appendix II).

Component 2

Control F1 Females

Fifteen untreated F1 females 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 bisphenol A, ketoconazole, and propylthiouracil. Fourteen of these animals survived to scheduled necropsy (see below).

In-Life Data from F1 Females Treated with Bisphenol A

Fifteen untreated F1 females were assigned to the 0, 400, or 600 mg/kg/day bisphenol A groups (Table 2-D). One animal in the control and high-dose groups, and 4 animals in the low-dose group were either found dead or euthanized due to moribundity prior to scheduled necropsy. Thus, 14, 11, and 14 females in the control, low, and high-dose groups were available for full evaluation in this study. Body weight at weaning (pnd 21) and on the day of initiation of dosing (pnd 22) was equivalent across treatment groups (Table 3-D). Daily body weights for F1 females were not significantly affected by treatment from pnd 23 to 25. Thereafter, body weight was significantly decreased in the high-dose group compared to the control group from pnd 26 to scheduled necropsy on pnd 42 or 43. In the low-dose group, body weight was decreased compared to the control group on pnd 29 and from pnd 31 to scheduled necropsy. Body weight change was equivalent across treatment groups for pnd 21 to 22. However, body weight change was less in the bisphenol A-treated groups at all time intervals except for pnd 42 to 43. This decrease was significant in both bisphenol A-treated groups compared to the control group for pnd 28 to 34, 34 to 40, 22 to 42, and 22 to 43, and also in the high-dose group for pnd 22 to 28 (Table 3-D).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) was equivalent across treatment groups and was not significantly affected by bisphenol A treatment on pnd 22 to 23, 26 to 27, 28 to 29, 29 to 30, and 42 to 43 (Table 4-D). The values for other intervals exhibited a significant dose-related decreasing trend. The low-dose bisphenol A-

treated groups exhibited a significant dose-related decrease in absolute feed consumption (by a range of 11.3% to 18.7%) on pnd 31 to 32, 32 to 33, 34 to 35, 36 to 37, 37 to 38, 38 to 39, 39 to 40, 40 to 41, and 41 to 42. The high-dose group exhibited decreases in absolute feed consumption (by range of 11.6% to 22.0%) for pnd 23 to 24, 24 to 25, 25 to 26, 27 to 28, and from pnd 30 throughout the rest of the treatment period to pnd 42. Absolute feed consumption for the treatment periods (pnd 22 to 42 and pnd 22 to 43) exhibited a decreasing trend, with the high-dose group significantly below the control group for both intervals (by 14.5% and 12.6%, respectively) and the low-dose group significantly decreased for pnd 22 to 42 (by 11.8%). When feed consumption was calculated as a percent of body weight (g/kg/day), the effects were less striking. A decreasing trend was noted for pnd 23 to 24, 24 to 25, 25 to 26, 27 to 28, 32 to 33, 34 to 35, 37 to 38, and 38 to 39. The low-dose group was significantly below the control group only for pnd 37 to 38 (by 10%). The high-dose group exhibited a significant decrease compared to the control group on pnd 23 to 24, 25 to 26, 27 to 28, 37 to 38, and 38 to 39 (by a range of 9.5% to 14.0%). A significant increase in relative feed consumption was noted for pnd 42 to 43, with the high-dose group consuming 33.1% more feed per body weight (mg/kg/day) than the control group. For the entire period from pnd 22 to scheduled necropsy on pnd 42 or 43, relative feed consumption exhibited a decreasing trend with both bisphenol A-treated groups consuming significantly less feed compared to the control group, with the two treated groups exhibiting a similar decrease in consumption (4.2% to 5.5%; Table 4-D).

Clinical observations were noted in the bisphenol A-treated groups and included efflux of the dosing solution, gasping, rooting postdosing, and salivation prior to dosing in 1, 1, 7, and 12 animals in the low-dose group, respectively, efflux of dosing solution, piloerection, audible respiration, rooting postdosing, and salivation prior to dosing in 2, 1, 2, 15, and 10 animals in the high-dose group, respectively (Table 5-D).

Treatment with bisphenol A did not affect the average day of vaginal opening (32.3–33.0 days; Table 6-D). The average body weight on the day of acquisition of vaginal opening exhibited a decreasing trend, and animals in the high-dose group weighed significantly less than the control group. Treatment with bisphenol A did not significantly affect any other measure of puberty, including the average number of days or postnatal day from vaginal opening to first estrus, the number or percent of females cycling, the average number of days or postnatal day from vaginal opening to the start or end of the first cycle, or the average number of days spent in any phase of the cycle (Table 6-D). One female in the low-dose group was acyclic, although she exhibited vaginal opening and first estrus. Three females in the high-dose group were acyclic. It is not known whether these females would have ultimately exhibited cycling if the observation period had been extended beyond pnd 42/43 (Table 6-D).

Necropsy and Histopathological Data from F1 Females Treated with Bisphenol A

At necropsy, average body weight exhibited a dose-related decreasing trend, with the low and high-dose bisphenol A-treated groups significantly below the control group (Table 7-D). In addition, absolute liver, paired kidney, and paired ovary weights decreased in a dose-related manner, with both treated groups significantly below the control group. Absolute uterine weight (with or without fluid) exhibited a dose-related decreasing trend; the high-dose group was significantly depressed for uterine weight without fluid. Absolute paired adrenal gland weight exhibited a significant decreasing trend. There was no effect of bisphenol A treatment on absolute pituitary or thyroid gland weights. When organ weights were adjusted with respect to necropsy body weight, adjusted paired ovary weight exhibited a decreasing trend, but there were no other significant effects. Bisphenol A treatment had no significant effect on circulating T4 or TSH levels (Table 7-D).

Gross necropsy findings were minimal and included three animals in the control and high-dose groups with hydronephrosis (Table 8-D). Ovarian hypoplasia was observed in 3/14 animals at the high dose. These ovaries exhibited a complete absence of corpora lutea and an apparent reduction or absence of Graffian follicles (Appendix II). As noted above, absolute paired ovary weight was significantly decreased at the high dose, whereas adjusted (necropsy) paired ovarian weight exhibited a dose-related decreasing trend, only.

In-Life Data from F1 Females Treated with Ketoconazole

Fifteen untreated F1 females were assigned to the 0, 50, or 100 mg/kg/day ketoconazole group (Table 2-E). One animal in the control group died prior to scheduled necropsy. Thus, 14, 15, and 15 F1 females were available for evaluation in this study. Body weights at weaning (pnd 21), on the day of initiation of dosing (pnd 22), and on pnd 23 were equivalent across treatment groups (Table 3-E). Daily body weights for F1 females exhibited a decreasing trend from pnd 24 to scheduled necropsy on pnd 42. The high-dose group was significantly below the control group on pnd 25 through 35 and pnd 37 to pnd 42. Body weight change was not affected by treatment with ketoconazole for pnd 21 to 22, 28 to 34, 34 to 40, 42 to 43, and 22 to 43. However, body weight change was significantly less in the high dose ketoconazole-treated group compared to the control group for pnd 22 to 28, 40 to 42, and 22 to 42 (Table 3-E).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment) was equivalent across treatment groups (Table 4-E). A decreasing trend was observed for absolute feed consumption on pnd 24 to 25, 25 to 26, 27 to 28, 28 to 29, 30 to 31, 31 to 32, 32 to 33, 35 to 36, 37 to 38, 40 to 41, 41 to 42, and 22 to 42. Significant decreases compared to the control group were observed at the high dose of ketoconazole (10.5% to 22.4%) on pnd 24 to 25, 28 to

29, 30 to 31, 31 to 32, 35 to 36, 37 to 38, 40 to 41, 41 to 42, 22 to 42, and 22 to 43. When feed consumption was calculated as a percent of body weight (g/kg/day), feed consumption exhibited a decreasing trend for pnd 21 to 22 that was obviously not related to treatment. After initiation of treatment, decreasing trends were noted on pnd 24 to 25, 28 to 29, 30 to 31, 35 to 36, 37 to 38, 41 to 42, 22 to 42, and 22 to 43. The high-dose group consumed significantly less (4.0% to 17.4%) on pnd 24 to 25, 28 to 29, 30 to 31, 37 to 38, 41 to 42, 22 to 42, 22 to 43. A significant increase in relative feed consumption was observed on pnd 29 to 30 (for both ketoconazole-treated groups). On pnd 42 to 43, the low-dose value was increased compared to the control group value (Table 4-E).

Clinical observations noted in the ketoconazole-treated groups included efflux of dosing solution, rooting postdosing, and salivation prior to dosing in 1, 5, and 6 animal(s) in the high-dose group, respectively, and piloerection, rooting postdosing, and salivation prior to dosing in 1, 3, and 6 animal(s) in the low-dose group, respectively (Table 5-E).

Treatment with ketoconazole had no significant effect on the average postnatal day of vaginal opening (Table 6-E). In addition, ketoconazole treatment had no effect on the average postnatal day of first estrus or the average number of days from vaginal opening until first estrus, the percent of females cycling, the average number of days from vaginal opening until the start or end of the first cycle, or the average postnatal day of the start or end of the first cycle. The average number of days in estrus during the first cycle was significantly longer at the high-dose (1.5 days vs. 1.1 days for the controls). However, there was no other effect on the number of days spent in an individual phase of the cycle. One animal in the control group, two animals in the low-dose group, and four animals in the high-dose group did not cycle (Table 6-E).

Necropsy and Histopathological Data from F1 Females Treated with Ketoconazole

At necropsy, average body weight exhibited a dose-related decreasing trend, with the high-dose ketoconazole-treated group value significantly below the control group value (Table 7-E). Absolute paired adrenal gland weight exhibited an increasing trend, with both the low and the high dose ketoconazole groups significantly greater than the control group. Absolute paired ovary weight and uterine weight (with or without fluid) exhibited a dose-related decreasing trend, with the high-dose value significantly below the control group value. No significant treatment effect was observed for absolute pituitary, thyroid, or liver weights. When organ weights were adjusted with respect to necropsy body weight, liver, paired adrenal gland and paired kidney weights increased in a dose-related manner that was significant at both doses of ketoconazole. Adjusted uterine weights without fluid (but not with) exhibited a decreasing trend. Ketoconazole treatment had no significant effect on adjusted pituitary, thyroid gland, or paired ovary weights, or on T4 or TSH levels (Table 7-E).

Gross necropsy findings included eight animals in the low-dose group and five animals in the high-dose group with pale and/or enlarged adrenal glands, three animals in the control group and two animals in the low-dose group with hydronephrosis, and one animal in the low-dose group with a missing ovary (Table 8-E). Cytoplasmic vacuolization of the corpora lutea was observed in 9/15 (60%) of the females exposed to the high dose of ketoconazole (Appendix II). These ovaries exhibited vacuoles within the cytoplasm of the corpora luteal cells. The severity was judged by a comparison of the average number and size of the vacuolated cells expressed as a percentage of the area of the corpora lutea affected by vacuolization, i.e., minimal = 6-25%, mild = 26 to 50%, moderate = 51-75%, and marked = 76-100%. Based on these criteria, the nine animals were scored as: 1 minimal; 4 mild; 3 moderate; and 1 marked. In addition, 5/15 (33%) of the high-dose females exhibited mild ovarian hypoplasia (no corpora lutea present). Thus, these five animals could not be evaluated for corpora luteal cytoplasmic vacuolization. A total of 14/15 animals (93.3%) exhibited ovarian pathology. Subsequent evaluation of the low-dose group revealed that 12/15 females exhibited cytoplasmic vacuolization of the corpora lutea: 6 minimal, 4 mild, and 2 moderate. No animals exhibited ovarian hypoplasia. The absolute paired ovarian weight was significantly decreased at the high but not the low dose of ketoconazole whereas adjusted paired ovarian weight exhibited a decreasing trend. This change in organ weight likely reflects the ovarian hypoplasia observed in the high-dose animals.

In-Life Data from F1 Females Treated with Propylthiouracil

Fifteen untreated F1 females were assigned to the 0, 2, or 25 mg/kg/day propylthiouracil group (Table 2-F). One animal assigned to the control group was found dead prior to scheduled necropsy. Thus, there were 14, 15, and 15 F1 females available for evaluation in the control, low- and high-dose groups, respectively. Body weights were equivalent across treatment groups from pnd 21 to pnd 31 (Table 3-F). Thereafter, the high-dose group weighed significantly less than the control group. Body weight change did not differ among groups for pnd 21 to 22, 22 to 28, or 42 to 43. However, body weight change was significantly less at the high dose of propylthiouracil compared to the control group for pnd 28 to 34, 34 to 40, 40 to 42, 22 to 42, and 22 to 43 (Table 3-F).

Feed consumption (g/day) for pnd 21 to 22 (prior to initiation of treatment), and for pnd 22 to 23 was equivalent across treatment groups (Table 4-F). The high-dose propylthiouracil-treated group exhibited a significant decrease in absolute feed consumption (by 13.3% compared to the control group) on pnd 23-24, which may have been influenced by the initiation of gavage dosing. Thereafter, the high-dose group exhibited a decrease in absolute feed consumption (by 18.8–54.1%) for pnd 28 to 29 and from pnd 30 to the end of treatment, with the greater effect occurring during the latter days of dosing. Absolute feed consumption for the whole treatment period (pnd 22 to 42 or 43) was also significantly decreased at the high dose (by 26.3 and 25.8%,

respectively). Absolute feed consumption was significantly decreased in the low-dose group for pnd 37 to 38 but not at any other time interval. When feed consumption was calculated as a percent of body weight (g/kg/day), feed consumption exhibited a decrease at the high dose on pnd 23 to 24 (by 13.1%) and on pnd 28 to 29 (by 18.0%). The high-dose group was significantly less than the control group for all time points from pnd 30 to pnd 42 (13.3% to 37.5% of the control value). Although only a decreasing trend was noted for pnd 42 to 43, relative feed consumption for the whole treatment period (pnd 22 to 42 or 22 to 43) was significantly decreased at the high dose (by 15.3%-16.5%; Table 4-F).

Clinical observations were noted in the propylthiouracil-treated groups and included rooting postdosing in 3 animals at the low dose, and piloerection, rooting postdosing, and salivation prior to dosing in 1, 5, and 6 animal(s) in the high-dose group, respectively (Table 5-F).

Treatment with propylthiouracil had no significant effect on the average postnatal day of vaginal opening (Table 6-F). There were no other significant treatment-related effects on any measure of puberty that was examined in this study. Specifically, there was no effect on the average number of days from vaginal opening until first estrus, average postnatal day of first estrus, percent of females cycling, average number of days from vaginal opening until the start or end of the first cycle, average postnatal day of the start or end of the first cycle, or number of days in individual stages of the estrous cycle. Average body weight on the day of acquisition of vaginal opening exhibited a decreasing trend and overall treatment effect ($p<0.05$) (Table 6-F).

Necropsy and Histopathological Data from F1 Females Treated with Propylthiouracil

At necropsy, average body weight exhibited a dose-related decreasing trend, with the high-dose propylthiouracil-treated group significantly below the control group (Table 7-F). Absolute pituitary weight and uterine weight (with or without fluid) were unaffected by treatment. However, absolute weights for liver, paired adrenals, paired kidneys, and paired ovaries were decreased at the high dose, whereas thyroid weight was increased at both dose levels. When organ weights were adjusted with respect to necropsy body weight, thyroid weight exhibited a dose-related increase, with values from both propylthiouracil-treated groups significantly greater than the control group value (4.3- and 9.5-fold for the low and high dose, respectively). No other treatment-related differences were noted for any other adjusted organ weights. As expected, circulating T4 levels decreased in a dose-related manner with both propylthiouracil-treated groups significantly decreased compared to control values (59.0% and 86.3%, respectively). TSH levels were increased 5.4-fold and 12.6-fold in the low and high-dose propylthiouracil-treated groups, respectively, compared to the control group value (Table 7-F).

Gross necropsy findings included three, three, and one animals in the control-, low-, and high-dose groups, respectively, with hydronephrosis, and one animal each in the high-dose group with a misshapen kidney, enlarged or enlarged/reddened thyroid gland, or fluid-filled uterus (Table 8-F). All animals in the high-dose group exhibited thyroid follicular cell hypertrophy/hyperplasia, characterized by increased size and apparent number of follicular cells, reduction of follicular lumen size, the presence of pale-staining colloid, and reduction in or absence of follicular colloid in some cells (Appendix II). 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 in the high-dose group scored minimal, two animals scored mild, nine moderate, and four marked. Based on these results, the low-dose thyroids were also examined, revealing that all 15 animals at the low dose also exhibited thyroid hypertrophy/hyperplasia. As expected, the severity was somewhat less, with scores of 1 minimal, 13 mild, 1 moderate, and no markedly affected animals. These changes were reflected in the dose-related increases in adjusted thyroid weight at both dose levels.

DISCUSSION AND CONCLUSION

This study was designed to gather information describing the conduct and usefulness of the female pubertal assay, that has been designated as a required 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 female 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 (Goldman et al., 2000). As summarized in Goldman et al. (2000), the female 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 each of these areas, the following compounds were tested: atrazine (affects the hypothalamus-pituitary axis in female rats and ovulation); fenarimol (a weak aromatase inhibitor); methoxychlor (a xeno-estrogen through α-estrogen receptor, anti-estrogen through β-estrogen receptor, and an anti-androgen through androgen receptor-mediated mechanism); bisphenol A (a weak environmental estrogen which binds to both the α and β estrogen receptor); ketoconazole (inhibits steroidogenesis in both sexes); and propylthiouracil (affects the thyroid directly, causing hypothyroidism). With respect to the test compounds, the results of this study are discussed below on how the protocol performed.

Atrazine

Treatment with atrazine at 75 or 150 mg/kg/day affected onset of puberty. The mean postnatal day of vaginal opening exhibited a significant delay at the high dose (36.4 vs. 32.9 days for the control group). Body weight and body weight gain were both decreased at both dose levels. The average postnatal day of first estrus and average postnatal day of the end of the first cycle were delayed at the high dose level. The average postnatal day of the start of the first cycle was delayed at both dose levels. There was no significant effect of treatment on cycle length or uterine weight (with or without fluid) in the present study. No differences were noted in T4 or TSH levels, and no treatment-related histopathological changes were observed in the thyroid, ovary, or uterus. These results agree with those of Laws et al. (2000), in their evaluation of the pubertal effects of atrazine (0, 50, 100, or 200 mg/kg/day) on female Wistar rats, using this study design. Laws et al. (2000), found that age and weight at vaginal opening were the most reliable indicators of disrupted pubertal development, observed in the absence of persistent organ weight changes or histopathology. A less reliable indicator was estrus cyclicity during the first cycle, which is likely to be highly variable at onset, regardless of treatment. Laws et al. (2000), observed a reduced number of regular 4- or 5-day cycles at the two highest dose levels during the first 15 days after vaginal opening, but this effect was no longer evident in the Wistar rats by pnd 57–71. In addition, Laws et al. (2000), observed decreased uterine weight (without fluid) at both 100 and 200 mg/kg/day, an effect that was not observed in the present study.

Fenarimol

Increased TSH was observed at both 50 and 250 mg/kg/day and, as such, was the only target parameter to exhibit a significant effect at the low dose of fenarimol. Decreased T4 was observed at the high dose. These effects on thyroid hormone levels were supported by the observation of minimal follicular hypertrophy in 33% of the high-dose thyroids. Decreased time spent in proestrus, decreased body weight and body weight change, and decreased feed consumption were all observed at the high dose, as was decreased adjusted pituitary weight. Adjusted liver weight was significantly increased at both doses of fenarimol.

Methoxychlor

Accelerated vaginal opening was observed at both doses of methoxychlor. For the high-dose animals, decreased adjusted ovary weight was also observed. However, since there was no treatment effect on other adjusted organ weights, thyroid hormone levels, or histopathology, vaginal opening was the most sensitive indicator, occurring at the low dose in the absence of other effects.

Bisphenol A

The mean postnatal day of vaginal opening was not affected by bisphenol A treatment. However, the body weight of the high-dose animals was significantly reduced on the day of acquisition. Adjusted paired ovary weight exhibited a decreasing trend, accompanied by ovarian hypoplasia in 21% of the high-dose animals. No other significant treatment-related changes were noted.

Ketoconazole

The mean day of vaginal opening was not affected by ketoconazole treatment. In addition, ovarian pathology, that increased in incidence and severity with dose, was observed at both 50 and 100 mg/kg/day. Cytoplasmic vacuolization of the corpora lutea was observed in 12/15 and 9/15 of the low- and high-dose animals, respectively, with the five remaining animals in the high-dose group exhibiting a complete absence of corpora lutea.

Propylthiouracil

As expected, propylthiouracil produced a decease in circulating T4 and an increase in TSH and, increased adjusted thyroid weight and thyroid follicular cell hypertrophy/ hyperplasia at both 2 and 25 mg/kg/day. There was no significant effect of treatment on any parameter of female pubertal development. In addition, other than the thyroid, treatment with propylthiouracil did not affect adjusted organ weights. Thus, the effect of propylthiouracil, although potent with respect to the thyroid, did not adversely affect female pubertal development in this study design.

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PROTOCOL DEVIATIONS

Twenty-five deviations from the protocol were noted as follows:

1. For Component 1, some animals in the Rx Code 37738 group, and all females in the Rx Code 41133 group were dosed outside the allowed range of 0700–1000 a.m. The dosing time range for these females was 1001–1029, exceeding the 1000 a.m. termination time. This occurred on Saturday, October 5, 2002 (Rx Codes 37738 and 41133) and on Sunday, October 6, 2002 (Rx Code 41133). For Component 2, all animals were dosed late on November 29, 2002. Additional instances of late dosing occurred during the dosing period of November 27, 2002 to December 18, 2002. The dosing time range for these females was 10:01 a.m. to 12:02 p.m. The technician responsible for the weekend dosing was not as fast a doser as the weekday assigned dosing technician.

2. Dam 24, Rx Code 93970, received 0.66 ml on pnd 34; she should have received 0.32 ml. Error in reading dosing chart.

3. Dosing or Postdosing observations were inadvertently not recorded during Component 1 for: Dam 15 on pnd 26, Dam 50 on pnd 31, Dam 79 on pnd 25, Dam 93 on pnd 25, Dam 25 on pnd 25, Dam 87 on pnd 41, Dam 101 on pnd 24, Dam 67 on pnd 24, Dam 20 on pnd 35, Dam 82 on pnd 22, 25 and 42, Dam 98 on pnd 22. For Dam 82 on pnd 32, neither dosing or postdosing observations were recorded.

4. Dosing or postdosing observations were inadvertently not recorded during Component 2 for: Dam 28 on pnd 21 and 36, Dam 35 on pnd 35, Dam 86 on pnd 25, Dam 96 on pnd 43, Dam 98 on pnd 25, Dam 41 on pnd 26, Dam 69 on pnd 40, Dam 89 on pnd 35, Dam 93 on pnd 35, Dam 67 on pnd 33, Dam 100 on pnd 40, Dam 105 on pnd 40, Dam 7 on pnd 38, Dam 102 on pnd 42. In addition, for Dam 102 on pnd 42, the time of observation was not recorded.

5. Post-dosing observations on December 8, 14, and 15, 2002 were recorded at greater than 2 hours postdosing for some dams in Component 2. On December 6, 2002, the postdosing observation was conducted late for numerous animals in Component 2. Observations were 1 minute to 76 minutes late.

6. F1 Dam 1, Rx Code 63561, pituitary not saved for this unscheduled death because of autolysis.

7. F1 Dam 6, Rx Code 37738, the uterus was inadvertently fixed in formalin rather than Bouins.

8. The estrous cycle records did not have the eartag # listed on the forms. This was not done since the eartag is not used for confirmation of the animal's identity. Only the Dam # is on the slide to be evaluated.

9. Dam 53, Rx Code 93970, vaginal smear not taken on the day of necropsy.

10. The female pups that were selected as sentinels were selected arbitrarily from those pups not assigned to study, rather than randomly, as stated in the protocol.

11. In ARF Room 204, the relative humidity was outside of the range specified by the protocol in the following instances: September 17, 2002, 80.5% for 1 hour; October 9, 2002, 88% for 2 hours; November 25, 2002, 27.5% for 1 hour.

12. In ARF Room 204, the temperature was outside of the range specified by the protocol in the following instance: October 9, 2002, 81.1°F for 1 hour.

13. Animal 16, Rx Code 05498, the pituitary was inadvertently not saved at necropsy.

14. The female pups for Dam 70, Rx Code 41133 were inadvertently not weighed on pnd 0.

15. Females 42, 46, 52, 50 and 80, whose pnd 0 was November 5, 2002, inadvertently did not have their litters weighed, sexed, grossly examined, or recorded on pnd 14, i.e., November 19, 2002.

16. The thyroid with trachea was inadvertently not saved for Dam #97, Rx Code 63561.

17. Clinical observations were not recorded for Animal 58, Rx Code 63561, on pnd 35.

18. Dosing and clinical observations data forms for pnd 31-43 carry only the Dam numbers. The forms should also have the eartag numbers.

19. Most of the female pup body weights were greater than 40-50 g on pnd 21. The weights specified in the protocol were based on the Charles River weight chart. The pups at RTI gained more weight during lactation than expected. Thus, the female pups were between approximately 50 and 62 g when put on study.

20. The clinical observations for animal 14, Rx Code 87668, were not recorded on pnd 25.

21. Animal 35, Rx Code 87668 received 0.48 ml of dosing solution on pnd 29 instead of 0.38 ml.

22. Clinical observations were not recorded postdosing for animal 17, Rx 25517, on pnd 27; animal 5, Rx Code 48744 on pnd 36; animal 67, Rx Code 48744, pnd 31; animal 6, Rx Code 86070, pnd 33.

23. Postdosing observations were not recorded for Dam 97, Rx Code 63516, on pnd 25.

24. During the course of the study, more than one set of numbers was used to denote the individual treatment groups in the two components. A memo addressing this has been placed in the study records and at the beginning of Appendix I.

25. For a few animals, eartags were not routinely checked on a few days. Incorrect eartag numbers were recorded then corrected.

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

Julia D. George, Ph.D.
Study Director

2/24/04
Date

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
NA	NA	2-14-D-F Top R-1, R1 to R3	preship	15	14.0[c]	93.1 ± 1.27[e]
NA	NA	2-14-D-F Bott R-1, R1 to R3	preship	15	14.2[c]	94.7 ± 2.74[e]
NA	NA	2-14-E-F Top R-1, R1 to R3	preship	30	27.9[c]	93.0 ± 3.06[e]
NA	NA	2-14-E-F Bott R-1, R1 to R3	preship	30	28.2[c]	94.0 ± 3.25[e]
67607	Blue	WA2-14D-F 9-18vial	first day dosing	15	16.77[d]	112
67607	Blue	WA2-14D-F 9-24vial	first day dosing	15	16.93[d]	113
67607	Blue	WA2-14D-F 10-1 vial	first day dosing	15	16.90[d]	113
67607	Blue	WA2-14D-F 10-8 vial	first day dosing	15	16.44[d]	110
02227	Orange	WA2-14E-F 9-18 vial	first day dosing	30	32.95[d]	110
02227	Orange	WA2-14E-F 9-24 vial	first day dosing	30	32.64[d]	109
02227	Orange	WA2-14E-F 10-1 vial	first day dosing	30	32.28[d]	108
02227	Orange	WA2-14E-F 10-8 vial	first day dosing	30	32.11[d]	107
67607	Blue	WA2-14-D-F Rep2Jar	postdose	15	14.0[d]	93
02227	Orange	WA2-14-E-F Rep2Jar	postdose	30	27.8[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 22, 28, 35, and 42, 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 Fenarimol 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)
NA	NA	2-14-F-F Top R-1Fen to R-3Fen	preship	10	9.29[c]	92.9 ± 2.01[e]
NA	NA	2-14-F-F Bot R-1Fen to R-3Fen	preship	10	9.23[c]	92.3 ± 1.79[e]
NA	NA	2-14-G-F Top R-1Fen to R-3Fen	preship	50	45.2[c]	90.5 ± 3.14[e]
NA	NA	2-14-G-F Bot R-1Fen to R-3Fen	preship	50	46.6[c]	93.1 ± 3.84[e]
10935	Green	2-14-F-F 9-18vial	first day dosing	10	10.91[d]	109
10935	Green	2-14-F-F 9-24vial	first day dosing	10	10.95[d]	109
10935	Green	2-14-F-F 10-1vial	first day dosing	10	11.17[d]	112
10935	Green	2-14-F-F 10-8vial	first day dosing	10	11.55[d]	116
93970	Brown	2-14-G-F 9-18vial	first day dosing	50	49.88[d]	99.8
93970	Brown	2-14-G-F 9-24vial	first day dosing	50	54.63[d]	109
93970	Brown	2-14-G-F 10-1vial	first day dosing	50	54.70[d]	109
93970	Brown	2-14-G-F 10-8vial	first day dosing	50	55.59[d]	111
10935	Green	2-14-F-F Rep2Jar	postdosing	10	9.98[d]	100
93970	Brown	2-14-G-F Rep3Jar	postdosing	50	51.0[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 22, 28, 35, and 42, 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-C. 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)
NA	NA	2-14-B-F R-1 R-1 to R-3	preship	5	--	--
NA	NA	2-14-C-F R-1 R-1 to R-3	preship	10	9.36[c]	93.6 ± 2.06[e]
NA	NA	2-14-B-F R-2 R1 to R-3	preship	5	4.94[c]	98.8 ± 5.65[e]
NA	NA	2-14-C-F R-2 R1 to R3	preship	10	f	f
NA	NA	2-14-B-F R-3 R-1 to R-3	preship	5[g]	4.87[c]	97.5 ± 3.98[e]
37738	Red	WA2-14B-F 9-18 vial	first day dosing	5	4.61[d]	92
37738	Red	WA2-14B-F 9-24 vial	first day dosing	5	4.63[d]	93
37738	Red	WA2-14B-F 10-1 vial	first day dosing	5	4.79[d]	96
37738	Red	WA2-14B-F 10-8 vial	first day dosing	5	4.93[d]	99
41133	Purple	WA2-14C-F 9-18 vial	first day dosing	10	9.01[d]	90
41133	Purple	WA2-14C-F 9-24 vial	first day dosing	10	9.21[d]	92
41133	Purple	WA2-14C-F 10-1 vial	first day dosing	10	9.26[d]	93
41133	Purple	WA2-14C-F 10-8 vial	first day dosing	10	9.43[d]	94
37738	Red	WA2-14-B-F Rep1Jar	postdose	5	4.62[d]	92
37738	Red	WA2-14-B-F Rep2Jar	postdose	5	4.93[d]	99
41133	Purple	WA2-14-C-F Rep2Jar	postdose	10	9.34[d]	93

Table 1-C. Analyses of Methoxychlor Dose Formulations[a] (continued)

[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 22, 28, 35, and 42, 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] Formulation not analyzed.
[g] Only the 5 mg/ml dose concentration was formulated, to replace the R1 formulation that had unacceptable analytical results.

Table 1-D. Analyses of Bisphenol A 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)
NA	NA	WA2-14-W-F R-1 to R-3	preship	80	81.5[c]	102 ± 0.859[e]
NA	NA	WA2-14-X-F R-1 to R-3	preship	120	123[c]	102 ± 3.29[e]
05498	Orange	11-27 W-F R-1	first day dosing	80	83.4[d]	104
05498	Orange	12-03 W-F R-1	first day dosing	80	81.4[d]	102
05498	Orange	12-10 W-F R-1	first day dosing	80	87.5[d]	109
05498	Orange	12-17 W-F R-1	first day dosing	80	78.9[d]	99
25517	Green	11-27 X-F R-1	first day dosing	120	125[d]	104
25517	Green	12-03 X-F R-1	first day dosing	120	130[d]	108
25517	Green	12-10 X-F R-1	first day dosing	120	131[d]	109
25517	Green	12-17 X-F R-1	first day dosing	120	134[d]	112
05498	Orange	2-14-W-F Remain R2	postdose	80	80.1[d]	100
25517	Green	2-14-X-F Remain R2	postdose	120	119[d]	99

[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 22, 28, 35, and 42, 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 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)
NA	NA	2-14-Y-F Rep1 R1 to R3	preship	10	10.0[c]	100.0 ± 3.09[e]
NA	NA	2-14-Z-F Rep1 R1 to	preship	20	18.4[c]	92.0 ± 2.18[e]
97694	Yellow	2-14-Y-F 11-27-02	first day dosing	10	8.09[d]	81
97694	Yellow	2-14-Y-F 12-03-02	first day dosing	10	10.8[d]	108
97694	Yellow	2-14-Y-F 12-10-02	first day dosing	10	10.9[d]	109
97694	Yellow	2-14-Y-F 12-17-02	first day dosing	10	8.37[d]	84
48744	Purple	2-14-Z-F 11-27-02	first day dosing	20	19.2[d]	96
48744	Purple	2-14-Z-F 12-03-02	first day dosing	20	19.4[d]	97
48744	Purple	2-14-Z-F 12-10-02	first day dosing	20	20.5[d]	103
48744	Purple	2-14-Z-F 12-17-02	first day dosing	20	11.6[d]	58
97694	Yellow	2-14-y-f R-2, remainder	postdose	10	11.2[d]	112
48744	Purple	2-14-z-f R-2, remainder	postdose	20	21.9[d]	110

[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 22, 28, 35, and 42, 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 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)
NA	NA	2-14 T-F Rep1 R1 to R3	preship	0.4	0.447[c]	112.0 ± 4.7[e]
NA	NA	2-14 V-F Rep1 R1 to R3	preship	5.0	4.65[c]	93.0 ± 2.64[e]
86070	Red	In-Life 11-27 2-14 T-F	first day dosing	0.4	0.344[d]	86
86070	Red	In-Life 12-03 2-14 T-F	first day dosing	0.4	0.359[d]	90
86070	Red	In-Life 12-10 2-14 T-F	first day dosing	0.4	0.388[d]	97
86070	Red	In-Life 12-17 2-14 T-F	first day dosing	0.4	0.351[d]	88
13694	Black	In Life 11-27 2-14 V-F	first day dosing	5.0	4.95[d]	99
13694	Black	In-Life 12-03 2-14 V-F	first day dosing	5.0	5.19[d]	84
13694	Black	In-Life 12-10 2-14 V-F	first day dosing	5.0	4.90[d]	98
13694	Black	In-Life 12-17 2-14 V-F	first day dosing	5.0	3.69[d]	74
86070	Red	From RTI, 2-14-T-F Remainder	postdose	0.4	0.393[d]	98
13694	Black	From RTI 2-14-V-F Remainder	postdose	5.0	4.71[d]	94

[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 22, 28, 35, and 42, and after dosing was completed (postdose).
[c] n=3 for individual determinations.
[d] n=1 for individual determinations0
[e] Data are presented as mean % (± % relative standard deviation).

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

	Atrazine (mg/kg/day, po)		
	0	75	150
NO. OF FEMALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	0	0	0
Scheduled Sacrifice	15	15	15

Table 2-B. Summary of the Fate of the Fenarimol-Treated F_1 Females (page 1 of 1)

	Fenarimol (mg/kg/day, po)		
	0	50	250
NO. OF FEMALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	0	0	0
Scheduled Sacrifice	15	15	15

Table 2-C. Summary of the Fate of the Methoxychlor-Treated F_1 Females (page 1 of 1)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
NO. OF FEMALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	0	1[a]	0
Scheduled Sacrifice	15	14	15

[a]Animal 23 was found dead on the afternoon of postnatal day 38.

Table 2-D. Summary of the Fate of the Bisphenol A-Treated F_1 Females (page 1 of 1)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
NO. OF FEMALES ON STUDY	15	15	15
Phase of Study			
Post Wean Period	1[a]	4[b]	1[c]
Scheduled Sacrifice	14	11	14

[a]Animal 1 was found dead on the morning of postnatal day 40.
[b]Animal 16 was found dead on the morning of postnatal day 28; animal 27 was found dead after dosing on postnatal day 30; animal 59 was found dead on the morning of postnatal day 27; and animal 87 was euthanized moribund after dosing on postnatal day 34.
[c]Animal 46 was found dead after dosing on postnatal day 29.

Table 2-E. Summary of the Fate of the Ketoconazole-Treated F_1 Females (page 1 of 1)

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

[a]Animal 1 was found dead on the morning of postnatal day 40.

Table 2-F. Summary of the Fate of the Propylthiouracil-Treated F_1 Females (page 1 of 1)

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

[a]Animal 1 was found dead on the morning of postnatal day 40.

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 Females (page 1 of 4)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Females on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.39 ± 1.00 N=15	56.30 ± 1.00 N=15	56.19 ± 0.97 N=15
Body Weight (pnd 22) (g)[a]	58.42 ± 0.97 N=15	58.91 ± 1.16 N=15	58.55 ± 1.22 N=15
Body Weight (pnd 23) (g)[a]	64.23 ‡‡ ± 1.14 §§ N=15	62.42 ± 1.13 N=15	58.49 ** ± 1.22 N=15
Body Weight (pnd 24) (g)[a]	70.00 ‡‡‡ ± 1.18 §§§ N=15	67.94 ± 1.22 N=15	61.28 *** ± 1.24 N=15
Body Weight (pnd 25) (g)[a]	75.53 ‡‡‡ ± 1.30 §§§ N=15	72.76 ± 1.42 N=15	66.70 *** ± 1.12 N=15
Body Weight (pnd 26) (g)[a]	81.52 ‡‡‡ ± 1.46 §§§ N=15	78.46 ± 1.47 N=15	72.94 *** ± 1.08 N=15
Body Weight (pnd 27) (g)[a]	87.80 ‡‡‡ ± 1.55 §§§ N=15	83.62 ± 1.75 N=15	77.88 *** ± 1.33 N=15
Body Weight (pnd 28) (g)[a]	94.28 ‡‡‡ ± 1.71 §§§ N=15	89.63 ± 1.84 N=15	83.35 *** ± 1.36 N=15

(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 Females (page 2 of 4)

	Atrazine (mg/kg/day, po)		
	0	75	150
Body Weight (pnd 29) (g)[a]	99.60 ‡‡‡ ± 2.34 §§§ N=15	95.28 ± 1.87 N=15	88.48 *** ± 1.51 N=15
Body Weight (pnd 30) (g)[a]	107.47 ‡‡‡ ± 1.83 §§§ N=15	101.60 ± 2.13 N=15	94.49 *** ± 1.62 N=15
Body Weight (pnd 31) (g)[a]	114.11 ‡‡‡ ± 2.03 §§§ N=15	107.46 * ± 2.10 N=15	99.28 *** ± 1.94 N=15
Body Weight (pnd 32) (g)[a]	120.82 ‡‡‡ ± 2.15 §§§ N=15	113.80 ± 2.25 N=15	104.60 *** ± 2.23 N=15
Body Weight (pnd 33) (g)[a]	128.87 ‡‡‡ ± 2.20 §§§ N=15	120.97 * ± 2.31 N=15	111.50 *** ± 2.32 N=15
Body Weight (pnd 34) (g)[a]	135.64 ‡‡‡ ± 2.20 §§§ N=15	127.60 * ± 2.51 N=15	117.14 *** ± 2.45 N=15
Body Weight (pnd 35) (g)[a]	142.78 ‡‡‡ ± 2.48 §§§ N=15	134.03 * ± 2.65 N=15	122.65 *** ± 2.63 N=15
Body Weight (pnd 36) (g)[a]	150.26 ‡‡‡ ± 2.62 §§§ N=15	141.39 ± 2.82 N=15	129.36 *** ± 2.91 N=15
Body Weight (pnd 37) (g)[a]	156.70 ‡‡‡ ± 2.74 §§§ N=15	146.75 * ± 2.76 N=15	135.47 *** ± 2.87 N=15

(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 Females (page 3 of 4)

	Atrazine (mg/kg/day, po)		
	0	75	150
Body Weight (pnd 38) (g)[a]			
	162.74 ‡‡‡ ± 3.04 §§§ N=15	151.32 * ± 2.81 N=15	140.05 *** ± 2.85 N=15
Body Weight (pnd 39) (g)[a]			
	167.61 ‡‡‡ ± 3.18 §§§ N=15	157.19 * ± 3.01 N=15	145.31 *** ± 3.13 N=15
Body Weight (pnd 40) (g)[a]			
	173.13 ‡‡‡ ± 3.45 §§§ N=15	162.28 * ± 3.15 N=15	151.02 *** ± 3.31 N=15
Body Weight (pnd 41) (g)[a]			
	178.31 ‡‡‡ ± 3.55 §§§ N=15	166.91 * ± 2.85 N=15	155.93 *** ± 3.44 N=15
Body Weight (pnd 42) (g)[a]			
	183.39 ‡‡‡ ± 3.61 §§§ N=15	171.02 * ± 2.73 N=15	160.98 *** ± 3.06 N=15
Body Weight (pnd 43) (g)[a,b]			
	193.96 ‡ ± 8.10 § N=5	178.60 ± 3.14 N=5	173.23 * ± 3.05 N=5
Body Weight Change (pnd 21 to 22) (g)[a]			
	2.03 ± 0.45 N=15	2.60 ± 0.63 N=15	2.36 ± 0.50 N=15
Body Weight Change (pnd 22 to 28) (g)[a]			
	35.86 ‡‡‡ ± 0.95 §§§ N=15	30.73 *** ± 0.94 N=15	24.80 *** ± 0.78 N=15

(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 Females (page 4 of 4)

	Atrazine (mg/kg/day, po)		
	0	75	150
Body Weight Change (pnd 28 to 34) (g)[a]			
	41.36 ‡‡‡ ± 1.09 §§§ N=15	37.97 ± 1.12 N=15	33.80 *** ± 1.29 N=15
Body Weight Change (pnd 34 to 40) (g)[a]			
	37.49 ± 1.89 N=15	34.68 ± 1.26 N=15	33.87 ± 1.37 N=15
Body Weight Change (pnd 40 to 42) (g)[a]			
	10.26 ± 1.08 N=15	8.74 ± 0.90 N=15	9.97 ± 0.57 N=15
Body Weight Change (pnd 42 to 43) (g)[a,b]			
	6.08 ± 1.35 N=5	5.49 ± 1.62 N=5	4.14 ± 2.22 N=5
Body Weight Change (pnd 22 to 42, treatment period) (g)[a]			
	124.97 ‡‡‡ ± 3.00 §§§ N=15	112.12 ** ± 2.45 N=15	102.43 *** ± 2.29 N=15
Body Weight Change (pnd 22 to 43, treatment period) (g)[a,b]			
	132.80 ‡ ± 7.16 §§ N=5	116.57 ± 3.28 N=5	110.03 * ± 3.11 N=5

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
‡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 Fenarimol-Treated F_1 Females (page 1 of 4)

	Fenarimol (mg/kg/day, po)		
	0	50	250
No. of Females on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.39 ± 1.00 N=15	56.33 ± 0.93 N=15	56.30 ± 1.11 N=15
Body Weight (pnd 22) (g)[a]	58.42 ± 0.97 N=15	59.44 ± 1.06 N=15	58.56 ± 1.43 N=15
Body Weight (pnd 23) (g)[a]	64.23 ‡‡‡ ± 1.14 §§§ N=15	63.50 ± 1.03 N=15	57.39 *** ± 1.35 N=15
Body Weight (pnd 24) (g)[a]	70.00 ‡‡‡ ± 1.18 §§§ N=15	69.71 ± 1.18 N=15	56.57 *** ± 1.32 N=15
Body Weight (pnd 25) (g)[a]	75.53 ‡‡‡ ± 1.30 §§§ N=15	75.84 ± 1.23 N=15	57.32 *** ± 1.22 N=15
Body Weight (pnd 26) (g)[a]	81.52 ‡‡‡ ± 1.46 §§§ N=15	81.80 ± 1.22 N=15	63.01 *** ± 1.47 N=15
Body Weight (pnd 27) (g)[a]	87.80 ‡‡‡ ± 1.55 §§§ N=15	87.29 ± 1.37 N=15	71.60 *** ± 1.52 N=15
Body Weight (pnd 28) (g)[a]	94.28 ‡‡‡ ± 1.71 §§§ N=15	93.33 ± 1.29 N=15	78.34 *** ± 1.64 N=15

(continued)

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 2 of 4)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Body Weight (pnd 29) (g)[a]	99.60 ‡‡‡ ± 2.34 §§§ N=15	100.19 ± 1.58 N=15	83.67 *** ± 1.77 N=15
Body Weight (pnd 30) (g)[a]	107.47 ‡‡‡ ± 1.83 §§§ N=15	106.65 ± 1.72 N=15	88.05 *** ± 1.83 N=15
Body Weight (pnd 31) (g)[a]	114.11 ‡‡‡ ± 2.03 §§§ N=15	113.07 ± 1.91 N=15	93.36 *** ± 1.95 N=15
Body Weight (pnd 32) (g)[a]	120.82 ‡‡‡ ± 2.15 §§§ N=15	121.94 ± 1.66 N=14[b]	99.35 *** ± 2.10 N=15
Body Weight (pnd 33) (g)[a]	128.87 ‡‡‡ ± 2.20 §§§ N=15	127.85 ± 2.27 N=15	106.09 *** ± 2.15 N=15
Body Weight (pnd 34) (g)[a]	135.64 ‡‡‡ ± 2.20 §§§ N=15	135.82 ± 2.38 N=15	112.69 *** ± 2.23 N=15
Body Weight (pnd 35) (g)[a]	142.78 ‡‡‡ ± 2.48 §§§ N=15	142.87 ± 2.48 N=15	119.40 *** ± 2.44 N=15
Body Weight (pnd 36) (g)[a]	150.26 ‡‡‡ ± 2.62 §§§ N=15	150.21 ± 2.43 N=15	125.94 *** ± 2.74 N=15
Body Weight (pnd 37) (g)[a]	156.70 ‡‡‡ ± 2.74 §§§ N=15	158.05 ± 2.66 N=15	133.05 *** ± 2.86 N=15

(continued)

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 3 of 4)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Body Weight (pnd 38) (g)[a]	162.74 ‡‡‡ ± 3.04 §§§ N=15	163.62 ± 2.67 N=15	139.37 *** ± 2.81 N=15
Body Weight (pnd 39) (g)[a]	167.61 ‡‡‡ ± 3.18 §§§ N=15	168.97 ± 2.63 N=15	146.27 *** ± 3.32 N=15
Body Weight (pnd 40) (g)[a]	173.13 ‡‡‡ ± 3.45 §§§ N=15	176.08 ± 2.94 N=15	153.03 *** ± 3.18 N=15
Body Weight (pnd 41) (g)[a]	178.31 ‡‡‡ ± 3.55 §§§ N=15	182.84 ± 2.90 N=15	158.98 *** ± 3.42 N=15
Body Weight (pnd 42) (g)[a]	183.39 ‡‡‡ ± 3.61 §§§ N=15	186.32 ± 2.93 N=15	166.48 ** ± 3.51 N=15
Body Weight (pnd 43) (g)[a,c]	193.96 ± 8.10 N=5	196.07 ± 3.36 N=5	181.08 ± 5.83 N=5
Body Weight Change (pnd 21 to 22) (g)[a]	2.03 ± 0.45 N=15	3.11 ± 0.35 N=15	2.26 ± 0.52 N=15
Body Weight Change (pnd 22 to 28) (g)[a]	35.86 ‡‡‡ ± 0.95 §§§ N=15	33.88 ± 0.71 N=15	19.78 *** ± 0.97 N=15

(continued)

Table 3-B. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 4 of 4)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Body Weight Change (pnd 28 to 34) (g)[a]			
	41.36 ‡‡‡ ± 1.09 §§§ N=15	42.49 ± 1.25 N=15	34.35 *** ± 0.81 N=15
Body Weight Change (pnd 34 to 40) (g)[a]			
	37.49 ± 1.89 N=15	40.26 ± 1.16 N=15	40.35 ± 1.37 N=15
Body Weight Change (pnd 40 to 42) (g)[a]			
	10.26 ‡ ± 1.08 § N=15	10.25 ± 0.98 N=15	13.45 * ± 0.88 N=15
Body Weight Change (pnd 42 to 43) (g)[a,c]			
	6.08 ± 1.35 N=5	4.50 ± 2.35 N=5	8.82 ± 0.95 N=5
Body Weight Change (pnd 22 to 42, treatment period) (g)[a]			
	124.97 ‡‡‡ ± 3.00 §§§ N=15	126.88 ± 2.77 N=15	107.92 *** ± 2.81 N=15
Body Weight Change (pnd 22 to 43, treatment period) (g)[a,c]			
	132.80 ± 7.16 N=5	132.90 ± 3.63 N=5	117.58 ± 6.47 N=5

[a] Reported as the mean ± S.E.M.; pnd = postnatal day.
[b] Decrease in N is due to the body weight on postnatal day 32 for female 18 being excluded because she did not have a water bottle between postnatal days 31 and 32.
[c] Includes those animals that were not scheduled for sacrifice until postnatal day 43.
‡ $p \leq 0.05$; ANOVA Test.
‡‡‡ $p < 0.001$; ANOVA Test.
§ $p \leq 0.05$; 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.

Table 3-C. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Methoxychlor-Treated F_1 Females (page 1 of 4)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Females on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.39 ± 1.00 N=15	56.12 ± 0.94 N=15	55.67 ± 1.05 N=15
Body Weight (pnd 22) (g)[a]	58.42 ± 0.97 N=15	58.73 ± 1.08 N=15	58.44 ± 1.21 N=15
Body Weight (pnd 23) (g)[a]	64.23 ± 1.14 N=15	63.97 ± 1.19 N=15	63.67 ± 1.23 N=15
Body Weight (pnd 24) (g)[a]	70.00 ± 1.18 N=15	69.60 ± 1.27 N=15	69.64 ± 1.29 N=15
Body Weight (pnd 25) (g)[a]	75.53 ± 1.30 N=15	75.63 ± 1.30 N=15	75.58 ± 1.38 N=15
Body Weight (pnd 26) (g)[a]	81.52 ± 1.46 N=15	81.48 ± 1.39 N=15	81.33 ± 1.49 N=15
Body Weight (pnd 27) (g)[a]	87.80 ± 1.55 N=15	87.07 ± 1.50 N=15	87.42 ± 1.47 N=15
Body Weight (pnd 28) (g)[a]	94.28 ± 1.71 N=15	93.15 ± 1.62 N=15	93.01 ± 1.52 N=15

(continued)

Table 3-C. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Methoxychlor-Treated F_1 Females (page 2 of 4)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Body Weight (pnd 29) (g)[a]	99.60 ± 2.34 N=15	99.37 ± 1.77 N=15	99.59 ± 1.69 N=15
Body Weight (pnd 30) (g)[a]	107.47 ± 1.83 N=15	105.65 ± 1.80 N=15	105.93 ± 1.68 N=15
Body Weight (pnd 31) (g)[a]	114.11 ± 2.03 N=15	111.97 ± 1.77 N=15	111.58 ± 1.76 N=15
Body Weight (pnd 32) (g)[a]	120.82 ± 2.15 N=15	118.91 ± 2.10 N=15	118.10 ± 2.05 N=15
Body Weight (pnd 33) (g)[a]	128.87 ± 2.20 N=15	125.01 ± 1.92 N=15	124.25 ± 2.03 N=15
Body Weight (pnd 34) (g)[a]	135.64 ± 2.20 N=15	131.15 ± 2.04 N=15	130.47 ± 2.07 N=15
Body Weight (pnd 35) (g)[a]	142.78 ± 2.48 **§** N=15	137.38 ± 1.96 N=15	136.12 ± 2.17 N=15
Body Weight (pnd 36) (g)[a]	150.26 ‡ ± 2.62 **§** N=15	144.00 ± 2.27 N=15	141.90 ***** ± 2.36 N=15
Body Weight (pnd 37) (g)[a]	156.70 ‡ ± 2.74 **§** N=15	150.60 ± 2.41 N=15	147.22 ***** ± 2.36 N=15

(continued)

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

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Body Weight (pnd 38) (g)[a]	162.74 ‡ ± 3.04 §§ N=15	155.16 ± 2.58 N=15	152.49 * ± 2.10 N=15
Body Weight (pnd 39) (g)[a]	167.61 ‡ ± 3.18 §§ N=15	159.87 ± 2.68 N=14[b]	157.40 * ± 2.17 N=15
Body Weight (pnd 40) (g)[a]	173.13 ‡ ± 3.45 §§ N=15	165.47 ± 2.61 N=14	161.42 ** ± 2.22 N=15
Body Weight (pnd 41) (g)[a]	178.31 ‡ ± 3.55 §§ N=15	169.41 ± 2.44 N=14	166.98 * ± 2.52 N=15
Body Weight (pnd 42) (g)[a]	183.39 ‡ ± 3.61 §§ N=15	174.38 ± 2.87 N=14	171.62 * ± 2.59 N=15
Body Weight (pnd 43) (g)[a,c]	193.96 ± 8.10 § N=5	179.52 ± 5.50 N=5	174.51 ± 2.91 N=6
Body Weight Change (pnd 21 to 22) (g)[a]	2.03 ± 0.45 N=15	2.61 ± 0.26 N=15	2.77 ± 0.31 N=15
Body Weight Change (pnd 22 to 28) (g)[a]	35.86 ± 0.95 N=15	34.42 ± 1.05 N=15	34.57 ± 0.72 N=15

(continued)

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

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Body Weight Change (pnd 28 to 34) (g)[a]	41.36 ‡ ± 1.09 §§ N=15	38.00 * ± 0.69 N=15	37.46 * ± 1.15 N=15
Body Weight Change (pnd 34 to 40) (g)[a]	37.49 ‡‡ ± 1.89 §§ N=15	34.54 ± 1.25 N=14[b]	30.95 ** ± 0.96 N=15
Body Weight Change (pnd 40 to 42) (g)[a]	10.26 ± 1.08 N=15	8.91 ± 0.78 N=14	10.20 ± 1.11 N=15
Body Weight Change (pnd 42 to 43) (g)[a,c]	6.08 ‡‡ ± 1.35 §§ N=5	-1.28 ** ± 1.38 N=5	-0.22 ** ± 0.63 N=6
Body Weight Change (pnd 22 to 42, treatment period) (g)[a]	124.97 ‡‡ ± 3.00 §§ N=15	115.57 * ± 2.17 N=14	113.18 ** ± 2.52 N=15
Body Weight Change (pnd 22 to 43, treatment period) (g)[a,c]	132.80 ‡ ± 7.16 §§ N=5	116.40 ± 4.85 N=5	111.79 * ± 2.25 N=6

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrease in N is due to animal 23 being found dead on the afternoon of postnatal day 38.
[c]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
‡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<0.05; Dunnett's 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 Bisphenol A-Treated F_1 Females (page 1 of 4)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
No. of Females on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.41 ± 0.81 N=15	56.31 ± 0.83 N=15	56.36 ± 0.86 N=15
Body Weight (pnd 22) (g)[a]	59.20 ± 0.81 N=15	58.48 ± 0.97 N=15	59.32 ± 0.82 N=15
Body Weight (pnd 23) (g)[a]	64.93 ± 0.84 N=15	64.14 ± 1.04 N=15	64.11 ± 0.98 N=15
Body Weight (pnd 24) (g)[a]	70.97 ± 0.88 N=15	69.24 ± 1.10 N=15	68.44 ± 0.85 N=15
Body Weight (pnd 25) (g)[a]	76.65 ± 1.19 **§** N=15	74.70 ± 1.18 N=15	73.12 ± 0.97 N=15
Body Weight (pnd 26) (g)[a]	82.11 **‡‡** ± 0.94 **§§** N=15	79.39 ± 1.36 N=15	76.44 ****** ± 1.21 N=15
Body Weight (pnd 27) (g)[a]	87.79 **‡‡** ± 1.13 **§§§** N=15	84.95 ± 1.47 N=14[b]	80.99 ****** ± 1.30 N=15
Body Weight (pnd 28) (g)[a]	93.73 **‡‡** ± 1.27 **§§§** N=15	90.11 ± 1.81 N=13[c]	85.78 ******* ± 1.36 N=15

(continued)

Table 3-D. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Bisphenol A-Treated F_1 Females (page 2 of 4)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Body Weight (pnd 29) (g)[a]	100.02 ‡‡‡ ± 1.30 §§§ N=15	94.76 * ± 1.90 N=13	91.24 *** ± 1.43 N=15
Body Weight (pnd 30) (g)[a]	106.72 ‡‡‡ ± 1.39 §§§ N=15	101.11 ± 2.18 N=13	96.07 *** ± 1.73 N=14[d]
Body Weight (pnd 31) (g)[a]	113.20 ‡‡‡ ± 1.63 §§§ N=15	105.72 * ± 2.21 N=12[e]	101.33 *** ± 1.94 N=14
Body Weight (pnd 32) (g)[a]	121.33 ‡‡‡ ± 1.78 §§§ N=15	111.60 ** ± 2.40 N=12	108.48 *** ± 2.01 N=14
Body Weight (pnd 33) (g)[a]	127.06 ‡‡‡ ± 1.82 §§§ N=15	116.95 ** ± 2.49 N=12	113.46 *** ± 1.92 N=14
Body Weight (pnd 34) (g)[a]	133.95 ‡‡‡ ± 1.84 §§§ N=15	123.47 ** ± 2.58 N=12	118.98 *** ± 2.11 N=14
Body Weight (pnd 35) (g)[a]	140.65 ‡‡‡ ± 2.00 §§§ N=15	127.36 *** ± 2.51 N=11[f]	122.27 *** ± 2.18 N=14
Body Weight (pnd 36) (g)[a]	145.47 ‡‡‡ ± 1.98 §§§ N=15	133.68 ** ± 2.57 N=11	126.82 *** ± 2.46 N=14
Body Weight (pnd 37) (g)[a]	152.77 ‡‡‡ ± 2.12 §§§ N=15	137.74 *** ± 2.74 N=11	132.53 *** ± 2.57 N=14

(continued)

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

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Body Weight (pnd 38) (g)[a]	159.36 ‡‡‡ ± 2.31 §§§ N=15	142.81 *** ± 2.84 N=11	137.66 *** ± 2.65 N=14
Body Weight (pnd 39) (g)[a]	165.63 ‡‡‡ ± 2.54 §§§ N=15	149.01 *** ± 2.86 N=11	142.52 *** ± 2.68 N=14
Body Weight (pnd 40) (g)[a]	171.07 ‡‡‡ ± 2.72 §§§ N=14[g]	152.91 *** ± 2.32 N=11	147.21 *** ± 2.86 N=14
Body Weight (pnd 41) (g)[a]	175.82 ‡‡‡ ± 2.83 §§§ N=14	156.48 *** ± 2.35 N=11	151.70 *** ± 2.86 N=14
Body Weight (pnd 42) (g)[a]	180.68 ‡‡‡ ± 2.84 §§§ N=14	160.21 *** ± 2.38 N=11	155.05 *** ± 2.91 N=14
Body Weight (pnd 43) (g)[a,h]	182.10 ‡‡ ± 3.75 §§§ N=6	170.15 * ± 3.70 N=5	160.88 *** ± 2.35 N=6
Body Weight Change (pnd 21 to 22) (g)[a]	2.78 ± 0.29 N=15	2.17 ± 0.35 N=15	2.96 ± 0.34 N=15
Body Weight Change (pnd 22 to 28) (g)[a]	34.54 ‡‡‡ ± 0.99 §§§ N=15	31.41 ± 1.12 N=13[b,c]	26.45 *** ± 1.20 N=15

(continued)

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

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Body Weight Change (pnd 28 to 34) (g)[a]	40.22 ‡‡‡ ± 0.83 §§§ N=15	34.06 *** ± 0.89 N=12[e]	33.38 *** ± 1.19 N=14[d]
Body Weight Change (pnd 34 to 40) (g)[a]	36.99 ‡‡‡ ± 1.70 §§§ N=14[g]	30.70 ** ± 0.65 N=11[f]	28.23 *** ± 1.43 N=14
Body Weight Change (pnd 40 to 42) (g)[a]	9.62 ± 0.80 § N=14	7.30 ± 0.55 N=11	7.83 ± 0.63 N=14
Body Weight Change (pnd 42 to 43) (g)[a,h]	3.42 ± 1.43 N=6	3.94 ± 1.27 N=5	4.57 ± 0.70 N=6
Body Weight Change (pnd 22 to 42, treatment period) (g)[a]	121.11 ‡‡‡ ± 2.79 §§§ N=14	101.82 *** ± 1.45 N=11	95.86 *** ± 2.50 N=14
Body Weight Change (pnd 22 to 43, treatment period) (g)[a,h]	120.20 ‡‡‡ ± 3.59 §§§ N=6	108.81 * ± 3.35 N=5	99.11 *** ± 1.94 N=6

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrease in N is due to animal 59 being found dead on the morning of postnatal day 27.
[c]Decrease in N is due to animal 16 being found dead on the morning of postnatal day 28.
[d]Decrease in N is due to animal 46 being found dead after dosing on postnatal day 29.
[e]Decrease in N is due to animal 27 being found dead after dosing on postnatal day 30.
[f]Decrease in N is due to animal 87 being euthanized moribund after dosing on postnatal day 34.
[g]Decrease in N is due to animal 1 being found dead on the morning of postnatal day 40.
[h]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
‡‡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-E. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Ketoconazole-Treated F_1 Females (page 1 of 4)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Females on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.41 ± 0.81 N=15	57.31 ± 0.93 N=15	56.46 ± 0.96 N=15
Body Weight (pnd 22) (g)[a]	59.20 ± 0.81 N=15	59.58 ± 1.21 N=15	58.96 ± 0.96 N=15
Body Weight (pnd 23) (g)[a]	64.93 ± 0.84 N=15	65.26 ± 1.12 N=15	63.00 ± 0.99 N=15
Body Weight (pnd 24) (g)[a]	70.97 ± 0.88 **§** N=15	70.26 ± 1.46 N=15	67.34 ± 0.89 N=15
Body Weight (pnd 25) (g)[a]	76.65 ‡ ± 1.19 **§** N=15	75.80 ± 1.63 N=15	72.00 ***** ± 1.14 N=15
Body Weight (pnd 26) (g)[a]	82.11 ‡ ± 0.94 **§§** N=15	81.73 ± 1.56 N=15	76.88 ***** ± 1.27 N=15
Body Weight (pnd 27) (g)[a]	87.79 ‡ ± 1.13 **§** N=15	87.22 ± 1.65 N=15	82.56 ***** ± 1.33 N=15
Body Weight (pnd 28) (g)[a]	93.73 ‡ ± 1.27 **§** N=15	93.60 ± 1.79 N=15	88.11 ***** ± 1.50 N=15

(continued)

Table 3-E. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Ketoconazole-Treated F_1 Females (page 2 of 4)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 29) (g)[a]	100.02 ‡ ± 1.30 §§ N=15	99.76 ± 1.82 N=15	93.66 * ± 1.60 N=15
Body Weight (pnd 30) (g)[a]	106.72 ‡ ± 1.39 § N=15	107.19 ± 2.27 N=15	99.84 * ± 2.00 N=15
Body Weight (pnd 31) (g)[a]	113.20 ‡‡ ± 1.63 §§ N=15	113.26 ± 2.01 N=15	105.57 * ± 2.08 N=15
Body Weight (pnd 32) (g)[a]	121.33 ‡ ± 1.78 §§ N=15	119.96 ± 2.01 N=15	112.79 * ± 2.37 N=15
Body Weight (pnd 33) (g)[a]	127.06 ‡ ± 1.82 § N=15	126.87 ± 2.10 N=15	118.90 * ± 2.47 N=15
Body Weight (pnd 34) (g)[a]	133.95 ‡ ± 1.84 § N=15	133.54 ± 2.24 N=15	125.89 * ± 2.73 N=15
Body Weight (pnd 35) (g)[a]	140.65 ‡ ± 2.00 § N=15	140.65 ± 2.17 N=15	131.66 * ± 2.77 N=15
Body Weight (pnd 36) (g)[a]	145.47 ‡ ± 1.98 § N=15	146.87 ± 2.38 N=15	137.71 ± 2.79 N=15
Body Weight (pnd 37) (g)[a]	152.77 ‡ ± 2.12 § N=15	152.73 ± 2.60 N=15	143.53 * ± 2.91 N=15

(continued)

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

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Body Weight (pnd 38) (g)[a]	159.36 ‡‡ ± 2.31 §§ N=15	158.83 ± 2.84 N=15	146.85 ** ± 2.68 N=15
Body Weight (pnd 39) (g)[a]	165.63 ‡‡ ± 2.54 §§ N=15	166.00 ± 2.85 N=15	152.78 ** ± 3.07 N=15
Body Weight (pnd 40) (g)[a]	171.07 ‡‡ ± 2.72 § N=14[b]	171.84 ± 3.00 N=15	159.85 * ± 2.92 N=15
Body Weight (pnd 41) (g)[a]	175.82 ‡‡ ± 2.83 §§ N=14	176.68 ± 3.00 N=15	162.88 ** ± 2.85 N=15
Body Weight (pnd 42) (g)[a]	180.68 ‡‡ ± 2.84 §§ N=14	181.12 ± 2.99 N=15	166.39 ** ± 2.96 N=15
Body Weight (pnd 43) (g)[a,c]	182.10 ± 3.75 N=6	188.64 ± 4.36 N=5	175.19 ± 4.17 N=5
Body Weight Change (pnd 21 to 22) (g)[a]	2.78 ± 0.29 N=15	2.27 ± 0.68 N=15	2.51 ± 0.20 N=15
Body Weight Change (pnd 22 to 28) (g)[a]	34.54 ‡‡ ± 0.99 §§ N=15	34.02 ± 0.92 N=15	29.15 ** ± 1.25 N=15

(continued)

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

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Body Weight Change (pnd 28 to 34) (g)[a]			
	40.22 ± 0.83 N=15	39.95 ± 0.80 N=15	37.78 ± 1.43 N=15
Body Weight Change (pnd 34 to 40) (g)[a]			
	36.99 ± 1.70 N=14[b]	38.30 ± 1.20 N=15	33.96 ± 0.96 N=15
Body Weight Change (pnd 40 to 42) (g)[a]			
	9.62 ‡ ± 0.80 § N=14	9.28 ± 0.81 N=15	6.54 * ± 0.99 N=15
Body Weight Change (pnd 42 to 43) (g)[a,c]			
	3.42 ± 1.43 N=6	5.59 ± 0.62 N=5	4.35 ± 0.97 N=5
Body Weight Change (pnd 22 to 42, treatment period) (g)[a]			
	121.11 ‡‡‡ ± 2.79 §§§ N=14	121.54 ± 2.11 N=15	107.42 *** ± 2.54 N=15
Body Weight Change (pnd 22 to 43, treatment period) (g)[a,c]			
	120.20 ± 3.59 N=6	126.81 ± 2.55 N=5	113.18 ± 3.74 N=5

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrease in N is due to animal 1 being found dead on the morning of postnatal day 40.
[c]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
‡$p<0.05$; 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-F. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Propylthiouracil-Treated F_1 Females (page 1 of 4)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Females on Study	15	15	15
Body Weight (pnd 21) (g)[a]	56.41 ± 0.81 N=15	56.44 ± 0.75 N=15	56.34 ± 0.85 N=15
Body Weight (pnd 22) (g)[a]	59.20 ± 0.81 N=15	58.84 ± 0.94 N=15	59.54 ± 0.87 N=15
Body Weight (pnd 23) (g)[a]	64.93 ± 0.84 N=15	64.64 ± 0.91 N=15	64.98 ± 0.88 N=15
Body Weight (pnd 24) (g)[a]	70.97 ± 0.88 N=15	70.29 ± 0.95 N=15	70.66 ± 0.80 N=15
Body Weight (pnd 25) (g)[a]	76.65 ± 1.19 N=15	75.80 ± 1.02 N=15	76.05 ± 0.89 N=15
Body Weight (pnd 26) (g)[a]	82.11 ± 0.94 N=15	81.64 ± 1.04 N=15	82.09 ± 0.98 N=15
Body Weight (pnd 27) (g)[a]	87.79 ± 1.13 N=15	87.44 ± 1.14 N=15	87.98 ± 1.02 N=15
Body Weight (pnd 28) (g)[a]	93.73 ± 1.27 N=15	93.15 ± 1.26 N=15	93.51 ± 1.10 N=15

(continued)

Table 3-F. Summary and Statistical Analysis of the Body Weights and Weight Changes During the Post Wean Period for the Propylthiouracil-Treated F_1 Females (page 2 of 4)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Body Weight (pnd 29) (g)[a]	100.02 ± 1.30 N=15	99.33 ± 1.34 N=15	99.10 ± 1.11 N=15
Body Weight (pnd 30) (g)[a]	106.72 ± 1.39 N=15	105.23 ± 1.48 N=15	104.39 ± 1.28 N=15
Body Weight (pnd 31) (g)[a]	113.20 ± 1.63 N=15	111.85 ± 1.62 N=15	109.50 ± 1.27 N=15
Body Weight (pnd 32) (g)[a]	121.33 ‡‡ ± 1.78 §§ N=15	119.47 ± 1.71 N=15	113.77 ** ± 1.54 N=15
Body Weight (pnd 33) (g)[a]	127.06 ‡‡‡ ± 1.82 §§§ N=15	125.97 ± 1.80 N=15	117.69 *** ± 1.56 N=15
Body Weight (pnd 34) (g)[a]	133.95 ‡‡‡ ± 1.84 §§§ N=15	132.15 ± 1.94 N=15	120.55 *** ± 1.51 N=15
Body Weight (pnd 35) (g)[a]	140.65 ‡‡‡ ± 2.00 §§§ N=15	138.58 ± 1.93 N=15	123.85 *** ± 1.71 N=15
Body Weight (pnd 36) (g)[a]	145.47 ‡‡‡ ± 1.98 §§§ N=15	144.09 ± 1.99 N=15	125.45 *** ± 1.91 N=15
Body Weight (pnd 37) (g)[a]	152.77 ‡‡‡ ± 2.12 §§§ N=15	147.34 ± 1.92 N=14[b]	126.50 *** ± 2.12 N=15

(continued)

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

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Body Weight (pnd 38) (g)[a]	159.36 ‡‡‡ ± 2.31 §§§ N=15	154.34 ± 1.93 N=15	127.09 *** ± 2.18 N=15
Body Weight (pnd 39) (g)[a]	165.63 ‡‡‡ ± 2.54 §§§ N=15	159.89 ± 2.11 N=15	128.22 *** ± 2.40 N=15
Body Weight (pnd 40) (g)[a]	171.07 ‡‡‡ ± 2.72 §§§ N=14[c]	166.53 ± 2.49 N=15	130.42 *** ± 2.47 N=15
Body Weight (pnd 41) (g)[a]	175.82 ‡‡‡ ± 2.83 §§§ N=14	171.14 ± 2.60 N=15	130.31 *** ± 2.85 N=15
Body Weight (pnd 42) (g)[a]	180.68 ‡‡‡ ± 2.84 §§§ N=14	175.77 ± 2.73 N=15	130.75 *** ± 2.57 N=15
Body Weight (pnd 43) (g)[a,d]	182.10 ‡‡‡ ± 3.75 §§§ N=6	181.15 ± 4.47 N=5	135.13 *** ± 5.62 N=5
Body Weight Change (pnd 21 to 22) (g)[a]	2.78 ± 0.29 N=15	2.41 ± 0.43 N=15	3.20 ± 0.34 N=15
Body Weight Change (pnd 22 to 28) (g)[a]	34.54 ± 0.99 N=15	34.31 ± 0.87 N=15	33.97 ± 0.74 N=15

(continued)

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

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Body Weight Change (pnd 28 to 34) (g)[a]			
	40.22 ‡‡‡ §§§ ± 0.83 N=15	39.00 ± 0.95 N=15	27.03 *** ± 1.11 N=15
Body Weight Change (pnd 34 to 40) (g)[a]			
	36.99 ‡‡‡ §§§ ± 1.70 N=14[c]	34.38 ± 1.50 N=15	9.87 *** ± 1.23 N=15
Body Weight Change (pnd 40 to 42) (g)[a]			
	9.62 ‡‡‡ §§§ ± 0.80 N=14	9.24 ± 0.68 N=15	0.33 *** ± 0.63 N=15
Body Weight Change (pnd 42 to 43) (g)[a,d]			
	3.42 ± 1.43 N=6	5.55 ± 1.07 N=5	0.62 ± 1.45 N=5
Body Weight Change (pnd 22 to 42, treatment period) (g)[a]			
	121.11 ‡‡‡ §§§ ± 2.79 N=14	116.93 ± 2.82 N=15	71.21 *** ± 2.18 N=15
Body Weight Change (pnd 22 to 43, treatment period) (g)[a,d]			
	120.20 ‡‡‡ §§§ ± 3.59 N=6	118.07 ± 3.78 N=5	72.39 *** ± 5.23 N=5

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Decrase in N is due to animal 101 being found outside of it's cage on the morning of postnatal day 37.
[c]Decrease in N is due to animal 1 being found dead on the morning of postnatal day 40.
[d]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
‡‡p<0.01; ANOVA Test.
‡‡‡p<0.001; ANOVA Test.
§§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.

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine-Treated F_1 Females (page 1 of 7)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Females on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	5.4 ± 0.2 N=15	5.3 ± 0.4 N=14[b]	5.7 ± 0.5 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	8.8 ‡‡‡ §§§ ± 0.3 N=14[b]	7.4 ** ± 0.2 N=15	5.4 *** ± 0.4 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	9.9 ‡‡‡ §§§ ± 0.2 N=15	9.1 ± 0.2 N=15	6.6 *** ± 0.4 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	11.2 ‡‡‡ §§§ ± 0.5 N=14[b]	10.1 ± 0.3 N=14[b]	8.7 *** ± 0.3 N=14[b]
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	11.8 ‡‡ §§ ± 0.3 N=13[b]	11.7 ± 0.3 N=14[c]	10.4 ** ± 0.3 N=14[c]
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	11.9 ± 0.6 § N=15	11.9 ± 0.3 N=15	10.6 ± 0.4 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
	13.3 ‡ § ± 0.4 N=14[b]	12.7 ± 0.4 N=15	11.9 * ± 0.3 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	13.6 ± 0.3 § N=14[c]	13.3 ± 0.4 N=15	12.6 ± 0.4 N=15

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine-Treated F_1 Females (page 2 of 7)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 29 to 30) (g/day)[a]	14.5 ± 0.4 § N=15	14.2 ± 0.5 N=15	13.2 ± 0.3 N=15
Feed Consumption (pnd 30 to 31) (g/day)[a]	14.1 ± 0.4 N=14[b]	14.2 ± 0.4 N=14[b]	13.6 ± 0.4 N=15
Feed Consumption (pnd 31 to 32) (g/day)[a]	15.7 ± 0.4 N=15	14.8 ± 0.6 N=15	14.6 ± 0.5 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]	16.6 ‡‡ ± 0.5 §§ N=15	16.0 ± 0.4 N=15	14.3 ** ± 0.5 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]	16.5 ± 0.5 N=15	16.6 ± 0.8 N=15	15.2 ± 0.6 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]	17.2 ± 0.5 § N=15	16.2 ± 0.6 N=15	15.4 ± 0.6 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]	17.9 ± 0.5 N=15	17.3 ± 0.8 N=15	16.6 ± 0.6 N=15
Feed Consumption (pnd 36 to 37) (g/day)[a]	18.1 ± 0.5 N=15	17.5 ± 0.5 N=15	17.2 ± 0.6 N=15
Feed Consumption (pnd 37 to 38) (g/day)[a]	18.5 ± 0.6 N=15	17.7 ± 0.5 N=15	17.3 ± 0.6 N=15

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine-Treated F_1 Females (page 3 of 7)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 38 to 39) (g/day)[a]			
	18.5 ± 0.6 N=15	19.2 ± 0.5 N=15	18.4 ± 0.7 N=15
Feed Consumption (pnd 39 to 40) (g/day)[a]			
	18.9 ± 0.6 N=15	18.2 ± 0.7 N=15	17.9 ± 0.5 N=15
Feed Consumption (pnd 40 to 41) (g/day)[a]			
	18.6 ± 0.6 N=15	18.6 ± 0.4 N=15	17.5 ± 0.9 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a,d]			
	18.4 ± 0.5 N=15	17.9 ± 0.6 N=15	17.3 ± 0.7 N=15
Feed Consumption (pnd 42 to 43) (g/day)[a,d]			
	18.5 ± 1.2 N=5	16.3 ± 0.8 N=5	18.0 ± 0.3 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/day)[a]			
	15.0 ± 0.4 § N=12[e]	14.6 ± 0.3 N=14[e]	13.8 ± 0.3 N=14[e]
Feed Consumption (pnd 22 to 43, treatment period) (g/day)[a,d]			
	15.2 ± 0.9 N=4[e]	14.9 ± 0.3 N=5	14.6 ± 0.5 N=5
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]			
	94.1 ± 3.9 N=15	91.1 ± 6.5 N=14[b]	98.3 ± 7.4 N=15

(continued)

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

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]			
#	144.3 †††	121.5 ÞÞÞ	92.8 ÞÞÞ
	± 2.4 ŸŸŸ	± 2.9	± 6.7
	N=14[b]	N=15	N=15
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
	147.4 ‡‡‡	140.4	110.8 ***
	± 2.1 §§§	± 2.9	± 5.8
	N=15	N=15	N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	154.4 ‡	143.9	135.3 **
	± 5.6 §§	± 3.4	± 3.7
	N=14[b]	N=14[b]	N=14[b]
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	152.2	156.0	148.8
	± 1.7	± 2.7	± 3.1
	N=13[b]	N=14[c]	N=14[c]
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	140.1	147.0	140.3
	± 6.2	± 2.8	± 4.6
	N=15	N=15	N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	146.1	147.4	147.9
	± 2.4	± 3.9	± 2.8
	N=14[b]	N=15	N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	141.5	144.1	146.1
	± 2.5	± 3.6	± 3.7
	N=14[c]	N=15	N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
	139.7	143.6	144.4
	± 2.8	± 3.9	± 2.1
	N=15	N=15	N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	126.8 ‡‡	136.5 *	140.1 **
	± 2.3 §§	± 2.7	± 3.2
	N=14[b]	N=14[b]	N=15

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine-Treated F_1 Females (page 5 of 7)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]			
	133.3 ± 2.8 N=15	133.9 ± 4.8 N=15	143.5 ± 4.6 N=15
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	132.8 ± 2.8 N=15	136.0 ± 2.4 N=15	132.8 ± 3.3 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	124.7 ± 2.6 N=15	132.6 ± 4.8 N=15	132.6 ± 4.1 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	123.1 ± 2.7 N=15	124.4 ± 4.1 N=15	128.7 ± 4.4 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	121.9 ± 2.5 N=15	125.4 ± 4.4 N=15	131.1 ± 3.4 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	117.7 ‡ ± 2.6 §§ N=15	121.2 ± 1.5 N=15	130.1 ** ± 3.9 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
#	115.5 ± 2.5 Ÿ N=15	118.5 ± 2.2 N=15	125.6 ± 3.7 N=15
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
	111.8 ‡‡‡ ± 2.7 §§§ N=15	124.4 ** ± 1.8 N=15	128.5 *** ± 3.7 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
	110.7 ± 2.1 § N=15	114.0 ± 3.7 N=15	121.6 ± 3.9 N=15

(continued)

Table 4-A. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Atrazine-Treated F_1 Females (page 6 of 7)

	Atrazine (mg/kg/day, po)		
	0	75	150
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
#	105.6 † ± 2.0 N=15	112.9 ÞÞ ± 1.7 N=15	114.2 ± 4.7 N=15
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
	101.4 ± 2.1 N=15	106.0 ± 2.4 N=15	108.9 ± 3.7 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[a,d]			
	97.0 ± 4.4 N=5	92.8 ± 3.5 N=5	105.3 ± 2.6 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/kg/day)[a]			
	124.9 ± 1.3 N=12[e]	128.1 ± 1.7 N=14[e]	129.4 ± 1.8 N=14[e]
Feed Consumption (pnd 22 to 43, treatment period) (g/kg/day)[a,d]			
	120.0 ± 3.0 N=4[e]	122.8 ± 2.1 N=5	126.5 ± 1.8 N=5

(continued)

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

[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]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
[e]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.
†$p<0.05$; 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.
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.

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 1 of 7)

	Fenarimol (mg/kg/day, po)		
	0	50	250
No. of Females on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	5.4 ± 0.2 **§** N=15	5.9 ± 0.2 N=15	6.2 ± 0.3 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	8.8 **‡‡‡** ± 0.3 **§§§** N=14[b]	8.4 ± 0.2 N=15	4.7 ******* ± 0.3 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	9.9 **‡‡‡** ± 0.2 **§§§** N=15	10.1 ± 0.2 N=15	3.9 ******* ± 0.3 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	11.2 **‡‡‡** ± 0.5 **§§§** N=14[b]	11.5 ± 0.2 N=15	4.9 ******* ± 0.2 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
#	11.8 **†††** ± 0.3 **ŸŸŸ** N=13[b]	12.6 ± 0.3 N=14[b]	8.7 **ÞÞÞ** ± 0.6 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	11.9 ± 0.6 N=15	12.4 ± 0.3 N=14[b]	11.2 ± 0.4 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
	13.3 ± 0.4 **§** N=14[b]	13.5 ± 0.2 N=14[b]	12.2 ± 0.6 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	13.6 ± 0.3 N=14[c]	14.1 ± 0.7 N=15	12.8 ± 0.4 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 2 of 7)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Feed Consumption (pnd 29 to 30) (g/day)[a]	14.5 ‡‡ ± 0.4 §§§ N=15	14.3 ± 0.4 N=15	12.4 ** ± 0.5 N=15
Feed Consumption (pnd 30 to 31) (g/day)[a]	14.1 ± 0.4 N=14[b]	16.6 ± 1.0 N=15	15.3 ± 1.0 N=15
Feed Consumption (pnd 31 to 32) (g/day)[a]	15.7 ± 0.4 § N=15	16.4 ± 0.5 N=14[d]	14.4 ± 0.7 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]	16.6 ‡‡‡ ± 0.5 §§§ N=15	15.9 ± 0.4 N=15	13.9 *** ± 0.3 N=14[b]
Feed Consumption (pnd 33 to 34) (g/day)[a]	16.5 ‡ ± 0.5 § N=15	17.3 ± 0.5 N=15	15.3 ± 0.6 N=14[c]
Feed Consumption (pnd 34 to 35) (g/day)[a]	17.2 ± 0.5 N=15	17.5 ± 0.5 N=14[b]	15.8 ± 0.7 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]	17.9 ‡‡ ± 0.5 §§ N=15	18.0 ± 0.4 N=15	15.5 * ± 0.8 N=15
Feed Consumption (pnd 36 to 37) (g/day)[a]	18.1 ± 0.5 N=15	18.2 ± 0.6 N=15	17.2 ± 1.0 N=15
Feed Consumption (pnd 37 to 38) (g/day)[a]	18.5 ± 0.6 N=15	18.9 ± 0.5 N=15	18.1 ± 0.7 N=14[b]

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 3 of 7)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Feed Consumption (pnd 38 to 39) (g/day)[a]			
	18.5 ± 0.6 N=15	18.9 ± 0.6 N=15	19.0 ± 1.1 N=15
Feed Consumption (pnd 39 to 40) (g/day)[a]			
	18.9 ± 0.6 N=15	20.0 ± 0.6 N=15	19.0 ± 0.7 N=15
Feed Consumption (pnd 40 to 41) (g/day)[a]			
	18.6 ± 0.6 N=15	19.4 ± 0.6 N=15	18.2 ± 0.7 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a]			
#	18.4 ± 0.5 N=15	17.3 ± 0.5 N=15	17.5 ± 1.0 N=14[b]
Feed Consumption (pnd 42 to 43) (g/day)[a,e]			
	18.5 ± 1.2 N=5	17.0 ± 1.3 N=5	19.0 ± 1.5 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/day)[a]			
	15.0 ‡‡‡ ± 0.4 §§§ N=12[f]	15.6 ± 0.3 N=12[f]	13.4 ** ± 0.4 N=13[f]
Feed Consumption (pnd 22 to 43, treatment period) (g/day)[a,e]			
	15.2 ± 0.9 N=4[f]	16.3 ± 0.2 N=4[f]	14.4 ± 0.4 N=5
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]			
	94.1 ± 3.9 § N=15	102.3 ± 4.3 N=15	108.9 ± 4.9 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 4 of 7)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]			
	144.3 ‡‡‡ ± 2.4 §§§ N=14[b]	136.7 ± 2.2 N=15	82.2 *** ± 4.2 N=15
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
#	147.4 ††† ± 2.1 ŸŸŸ N=15	151.8 ± 2.2 N=15	68.7 ÞÞÞ ± 4.6 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	154.4 ‡‡‡ ± 5.6 §§§ N=14[b]	157.8 ± 2.8 N=15	87.0 *** ± 3.9 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
#	152.2 † ± 1.7 N=13[b]	160.2 Þ ± 2.6 N=14[b]	143.4 ± 9.0 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	140.1 ‡‡‡ ± 6.2 §§§ N=15	147.3 ± 3.0 N=14[b]	165.8 *** ± 3.7 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	146.1 ‡ ± 2.4 § N=14[b]	150.3 ± 2.6 N=14[b]	163.1 * ± 7.2 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	141.5 ‡ ± 2.5 §§ N=14[c]	145.4 ± 5.6 N=15	157.3 * ± 3.4 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
#	139.7 ± 2.8 N=15	138.1 ± 3.0 N=15	144.8 ± 5.6 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	126.8 ‡‡‡ ± 2.3 §§§ N=14[b]	150.7 * ± 7.4 N=15	166.7 *** ± 8.2 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 5 of 7)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]			
	133.3 ± 2.8 § N=15	138.4 ± 3.5 N=14[d]	151.4 ± 8.6 N=15
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	132.8 ‡ ± 2.8 N=15	127.5 ± 2.2 N=14[d]	135.9 ± 1.8 N=14
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	124.7 ‡‡ ± 2.6 §§§ N=15	131.0 ± 2.4 N=15	140.1 *** ± 3.5 N=14[c]
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	123.1 ‡ ± 2.7 §§ N=15	126.1 ± 2.0 N=14[b]	136.1 * ± 4.7 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	121.9 ± 2.5 N=15	122.7 ± 1.5 N=15	126.3 ± 6.0 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	117.7 ‡ ± 2.6 §§ N=15	118.0 ± 3.2 N=15	132.3 * ± 5.5 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
	115.5 ‡‡‡ ± 2.5 §§§ N=15	117.6 ± 2.0 N=15	133.1 *** ± 3.9 N=14[b]
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
#	111.8 † ± 2.7 ŸŸ N=15	113.5 ± 3.1 N=15	132.7 ÞÞ ± 6.7 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
#	110.7 †† ± 2.1 ŸŸ N=15	115.6 ± 2.4 N=15	127.1 ÞÞ ± 4.6 N=15

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 6 of 7)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
	105.6 ‡ § ± 2.0 N=15	108.3 ± 3.1 N=15	116.4 * ± 3.9 N=15
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
#	101.4 †† ± 2.1 N=15	93.6 ÞÞ ± 1.7 N=15	107.7 ± 5.6 N=14[b]
Feed Consumption (pnd 42 to 43) (g/kg/day)[a,e]			
	97.0 ± 4.4 N=5	87.2 ± 5.7 N=5	107.5 ± 6.5 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/kg/day)[a]			
	124.9 ‡ § ± 1.3 N=12[f]	127.0 ± 1.1 N=12[f]	130.3 * ± 1.8 N=13[f]
Feed Consumption (pnd 22 to 43, treatment period) (g/kg/day)[a,e]			
	120.0 ‡ § ± 3.0 N=4[f]	123.6 ± 0.6 N=4[f]	129.1 * ± 2.1 N=5

(continued)

Table 4-B. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 7 of 7)

[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]Decrease in N is due to the body weight on postnatal day 32 and the feed consumption value for postnatal days 31-32 for female 18 being excluded because she did not have a water bottle between postnatal days 31 and 32.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
[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.
† $p<0.05$; 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.
††† $p<0.001$; 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.
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-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor-Treated F_1 Females (page 1 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Females on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	5.4 ± 0.2 N=15	6.3 ± 0.3 N=15	6.1 ± 0.4 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	8.8 ± 0.3 N=14[b]	9.0 ± 0.2 N=15	9.1 ± 0.2 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	9.9 ± 0.2 N=15	10.1 ± 0.3 N=15	10.3 ± 0.2 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	11.2 ± 0.5 N=14[b]	11.4 ± 0.3 N=14[b]	11.3 ± 0.2 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	11.8 ± 0.3 N=13[b]	12.6 ± 0.4 N=14[b]	12.7 ± 0.4 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	11.9 ± 0.6 N=15	12.6 ± 0.3 N=15	12.6 ± 0.4 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
	13.3 ± 0.4 N=14[b]	13.1 ± 0.4 N=15	12.8 ± 0.3 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	13.6 ± 0.3 N=14[c]	13.6 ± 0.3 N=15	13.8 ± 0.3 N=15

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor-Treated F_1 Females (page 2 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 29 to 30) (g/day)[a]	14.5 ± 0.4 N=15	13.8 ± 0.3 N=15	14.1 ± 0.3 N=15
Feed Consumption (pnd 30 to 31) (g/day)[a]	14.1 ± 0.4 N=14[b]	14.2 ± 0.4 N=14[c]	14.5 ± 0.3 N=15
Feed Consumption (pnd 31 to 32) (g/day)[a]	15.7 ± 0.4 N=15	15.2 ± 0.4 N=14[b]	15.2 ± 0.4 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]	16.6 ‡‡ ± 0.5 § N=15	15.1 * ± 0.3 N=15	15.1 * ± 0.3 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]	16.5 ± 0.5 N=15	16.2 ± 0.4 N=15	16.1 ± 0.5 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]	17.2 ± 0.5 N=15	16.4 ± 0.4 N=15	16.0 ± 0.5 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]	17.9 ‡ ± 0.5 § N=15	16.3 ± 0.5 N=15	15.9 * ± 0.6 N=15
Feed Consumption (pnd 36 to 37) (g/day)[a]	18.1 ‡ ± 0.5 §§ N=15	17.3 ± 0.6 N=15	16.1 * ± 0.5 N=15
Feed Consumption (pnd 37 to 38) (g/day)[a]	18.5 ± 0.6 N=15	16.9 ± 0.6 N=15	17.0 ± 0.4 N=15

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor-Treated F_1 Females (page 3 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 38 to 39) (g/day)[a]	18.5 ± 0.6 N=15	18.8 ± 0.6 N=14[d]	18.3 ± 0.4 N=15
Feed Consumption (pnd 39 to 40) (g/day)[a]	18.9 ± 0.6 § N=15	17.9 ± 0.6 N=14	16.6 ± 0.7 N=15
Feed Consumption (pnd 40 to 41) (g/day)[a]	18.6 ‡ ± 0.6 § N=15	16.9 * ± 0.2 N=14	16.7 * ± 0.6 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a]	18.4 ‡ ± 0.5 § N=15	16.4 * ± 0.7 N=14	16.2 * ± 0.4 N=15
Feed Consumption (pnd 42 to 43) (g/day)[a,e]	18.5 ‡‡‡ ± 1.2 §§ N=5	13.9 ** ± 0.6 N=5	13.6 *** ± 0.2 N=6
Feed Consumption (pnd 22 to 42, treatment period) (g/day)[a]	15.0 ± 0.4 N=12[f]	14.5 ± 0.3 N=12[f]	14.5 ± 0.2 N=15
Feed Consumption (pnd 22 to 43, treatment period) (g/day)[a,e]	15.2 ± 0.9 N=4[f]	15.0 ± 0.7 N=4[f]	14.4 ± 0.4 N=6
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	94.1 ± 3.9 N=15	108.2 ± 4.2 N=15	106.3 ± 6.0 N=15

(continued)

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

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]			
	144.3 ± 2.4 N=14[b]	146.2 ± 3.0 N=15	148.5 ± 2.0 N=15
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
	147.4 ‡ ± 2.1 § N=15	151.4 ± 2.2 N=15	155.3 * ± 2.2 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	154.4 ± 5.6 N=14[b]	157.8 ± 2.9 N=14[b]	155.7 ± 1.9 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	152.2 ‡ ± 1.7 § N=13[b]	161.5 ± 2.7 N=14[b]	161.6 * ± 3.6 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	140.1 ± 6.2 N=15	149.8 ± 3.5 N=15	150.4 ± 5.0 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	146.1 ± 2.4 N=14[b]	145.0 ± 2.9 N=15	142.0 ± 2.1 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	141.5 ± 2.5 N=14[c]	141.2 ± 1.8 N=15	143.2 ± 2.7 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
	139.7 ± 2.8 N=15	134.9 ± 2.3 N=15	137.0 ± 2.4 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	126.8 ± 2.3 N=14[b]	131.5 ± 3.1 N=14[c]	133.2 ± 2.2 N=15

(continued)

Table 4-C. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Methoxychlor-Treated F_1 Females (page 5 of 6)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]			
	133.3 ± 2.8 N=15	132.8 ± 2.8 N=14[b]	132.3 ± 2.1 N=15
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	132.8 ‡ ± 2.8 § N=15	123.7 * ± 2.3 N=15	125.0 ± 2.3 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	124.7 ± 2.6 N=15	126.6 ± 2.0 N=15	126.3 ± 3.4 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	123.1 ± 2.7 N=15	121.9 ± 2.2 N=15	120.0 ± 3.4 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	121.9 ± 2.5 § N=15	115.6 ± 1.8 N=15	113.8 ± 3.2 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	117.7 ± 2.6 N=15	117.0 ± 2.8 N=15	111.2 ± 2.8 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
	115.5 ± 2.5 N=15	110.3 ± 2.7 N=15	113.9 ± 2.9 N=15
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
	111.8 ± 2.7 N=15	119.4 ± 2.7 N=14[d]	118.3 ± 2.5 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
	110.7 ± 2.1 N=15	110.2 ± 3.2 N=14	104.2 ± 3.8 N=15

(continued)

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

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
#	105.6 ± 2.0 N=15	101.3 ± 1.0 N=14	102.0 ± 3.1 N=15
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
	101.4 ± 2.1 N=15	94.9 ± 3.1 N=14	96.2 ± 2.8 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[a,e]			
	97.0 ‡‡‡ ± 4.4 §§ N=5	76.9 ** ± 2.0 N=5	77.9 ** ± 2.3 N=6
Feed Consumption (pnd 22 to 42, treatment period) (g/kg/day)[a]			
	124.9 ± 1.3 N=12[f]	124.0 ± 1.1 N=12[f]	124.4 ± 1.2 N=15
Feed Consumption (pnd 22 to 43, treatment period) (g/kg/day)[a,e]			
	120.0 ± 3.0 N=4[f]	120.1 ± 1.6 N=4[f]	117.4 ± 1.3 N=6

[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]Decrease in N is due to animal 23 being found dead on the afternoon of postnatal day 38.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
[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.
*$p<0.05$; Dunnett's Test.
**$p<0.01$; Dunnett's Test.
***$p<0.001$; Dunnett's Test.

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Bisphenol A-Treated F_1 Females (page 1 of 7)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
No. of Females on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	7.7 ± 0.7 N=15	6.7 ± 0.6 N=15	8.0 ± 0.7 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	8.9 ± 0.4 N=15	9.6 ± 0.5 N=15	8.5 ± 0.6 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	10.5 ‡ §§ ± 0.5 N=15	9.0 ± 0.6 N=15	8.8 * ± 0.2 N=14[b]
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	11.6 ‡ §§ ± 0.6 N=15	10.9 ± 0.4 N=15	9.4 * ± 0.6 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	12.7 ‡‡ §§ ± 0.5 N=15	11.6 ± 0.4 N=15	10.5 ** ± 0.4 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	12.0 ± 0.5 N=15	12.3 ± 0.4 N=14[c]	10.9 ± 0.5 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
	13.4 ‡‡‡ §§§ ± 0.3 N=15	12.5 ± 0.4 N=12[b,d]	10.9 *** ± 0.6 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	14.9 ± 0.5 N=15	13.4 ± 0.6 N=12[e]	13.9 ± 0.7 N=15

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Bisphenol A-Treated F_1 Females (page 2 of 7)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Feed Consumption (pnd 29 to 30) (g/day)[a]	13.5 ± 0.7 N=15	13.4 ± 0.6 N=11[e,f]	11.7 ± 0.8 N=13[e,g]
Feed Consumption (pnd 30 to 31) (g/day)[a]	14.9 ‡ ± 0.5 §§ N=15	12.9 ± 0.6 N=11[b,h]	12.3 * ± 0.7 N=12[b,e]
Feed Consumption (pnd 31 to 32) (g/day)[a]	15.5 ‡‡ ± 0.4 §§ N=15	13.7 ** ± 0.5 N=12	13.7 * ± 0.4 N=12[b]
Feed Consumption (pnd 32 to 33) (g/day)[a]	15.4 ‡‡‡ ± 0.5 §§§ N=15	13.1 ** ± 0.5 N=12	12.7 *** ± 0.4 N=14
Feed Consumption (pnd 33 to 34) (g/day)[a]	16.5 ‡ ± 0.4 § N=15	15.0 ± 0.7 N=12	14.3 * ± 0.8 N=14
Feed Consumption (pnd 34 to 35) (g/day)[a]	16.9 ‡‡‡ ± 0.6 §§§ N=15	14.5 * ± 0.7 N=11[i]	13.4 *** ± 0.4 N=13[b]
Feed Consumption (pnd 35 to 36) (g/day)[a]	16.7 ‡‡‡ ± 0.5 §§§ N=15	15.2 ± 0.6 N=11	13.1 *** ± 0.8 N=14
Feed Consumption (pnd 36 to 37) (g/day)[a]	17.5 ‡‡ ± 0.6 §§ N=15	15.0 * ± 0.9 N=11	14.5 ** ± 0.6 N=14
Feed Consumption (pnd 37 to 38) (g/day)[a]	18.2 ‡‡‡ ± 0.6 §§§ N=15	14.8 *** ± 0.6 N=11	14.2 *** ± 0.5 N=14

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Bisphenol A-Treated F_1 Females (page 3 of 7)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Feed Consumption (pnd 38 to 39) (g/day)[a]	18.6 ‡‡‡ ± 0.6 §§§ N=15	16.5 * ± 0.6 N=11	14.5 *** ± 0.6 N=14
Feed Consumption (pnd 39 to 40) (g/day)[a]	18.6 ‡‡‡ ± 0.5 §§§ N=14[l]	16.0 ** ± 0.5 N=11	15.7 *** ± 0.6 N=14
Feed Consumption (pnd 40 to 41) (g/day)[a]	18.2 ‡‡‡ ± 0.4 §§§ N=14	15.8 ** ± 0.5 N=10[b]	15.0 *** ± 0.6 N=14
Feed Consumption (pnd 41 to 42) (g/day)[a]	18.5 ‡‡‡ ± 0.6 §§§ N=14	15.2 ** ± 0.8 N=10[e]	15.5 ** ± 0.5 N=14
Feed Consumption (pnd 42 to 43) (g/day)[a,k]	15.6 ± 0.2 N=5[b]	15.3 ± 0.8 N=4[b]	18.4 ± 1.6 N=6
Feed Consumption (pnd 22 to 42, treatment period) (g/day)[a]	15.2 ‡‡‡ ± 0.3 §§§ N=14	13.4 ** ± 0.4 N=8[l]	13.0 *** ± 0.3 N=11[l]
Feed Consumption (pnd 22 to 43, treatment period) (g/day)[a,k]	15.1 ‡ ± 0.5 §§ N=5[l]	13.6 ± 0.5 N=4[l]	13.2 * ± 0.2 N=5[l]
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	133.4 ± 12.1 N=15	115.8 ± 9.8 N=15	137.6 ± 10.6 N=15

(continued)

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

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]			
	144.1 ± 5.5 N=15	156.4 ± 6.2 N=15	138.5 ± 10.3 N=15
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
	153.9 ‡ ± 7.3 § N=15	133.8 ± 7.7 N=15	132.4 * ± 3.2 N=14[b]
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	156.5 ± 7.8 § N=15	152.3 ± 6.5 N=15	132.3 ± 7.7 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	159.5 ‡ ± 6.0 §§ N=15	150.1 ± 3.5 N=15	139.3 ** ± 4.5 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	140.6 ± 4.8 N=15	149.0 ± 3.2 N=14[c]	138.0 ± 6.4 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	147.4 ‡ ± 3.5 § N=15	143.1 ± 3.2 N=12[b,d]	130.4 * ± 6.2 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	153.9 ± 4.4 N=15	144.2 ± 3.9 N=12[e]	156.8 ± 6.7 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
	129.9 ± 5.9 N=15	135.3 ± 4.8 N=11[e,f]	124.9 ± 7.8 N=13[e,g]
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	135.0 ± 4.3 N=15	123.8 ± 4.8 N=11[b,h]	124.2 ± 6.7 N=12[b,e]

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Bisphenol A-Treated F_1 Females (page 5 of 7)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]	132.4 ± 2.6 N=15	125.6 ± 3.4 N=12	130.4 ± 3.3 N=12[b]
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]	124.1 ± 3.6 **§** N=15	114.9 ± 3.5 N=12	114.1 ± 3.5 N=14
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]	126.5 ± 2.1 N=15	124.2 ± 4.3 N=12	123.0 ± 5.7 N=14
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]	122.6 ± 3.3 **§** N=15	115.7 ± 4.6 N=11[i]	111.0 ± 2.4 N=13[b]
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]	116.8 ± 2.7 N=15	116.5 ± 4.0 N=11	104.4 ± 5.8 N=14
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]	117.1 ± 2.6 N=15	109.8 ± 5.2 N=11	111.4 ± 2.5 N=14
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]	116.6 **‡‡** ± 2.9 **§§** N=15	104.9 ***** ± 2.4 N=11	105.2 ****** ± 2.6 N=14
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]	114.1 **‡** ± 2.6 **§** N=15	112.7 ± 3.0 N=11	103.3 ****** ± 2.4 N=14
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]	110.7 ± 2.2 N=14[j]	106.5 ± 3.7 N=11	107.8 ± 2.9 N=14

(continued)

Table 4-D. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Bisphenol A-Treated F_1 Females (page 6 of 7)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
	104.9 ± 1.8 N=14	102.0 ± 3.7 N=10[b]	100.3 ± 2.7 N=14
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
	103.5 ± 2.9 N=14	95.2 ± 4.4 N=10[e]	100.9 ± 2.3 N=14
Feed Consumption (pnd 42 to 43) (g/kg/day)[a,k]			
	86.9 ‡ ± 1.8 § N=5[b]	91.5 ± 2.9 N=4[b]	115.7 * ± 9.8 N=6
Feed Consumption (pnd 22 to 42, treatment period) (g/kg/day)[a]			
	125.9 ‡‡ ± 1.3 §§§ N=14	119.5 ** ± 1.2 N=8[l]	119.0 ** ± 1.5 N=11[l]
Feed Consumption (pnd 22 to 43, treatment period) (g/kg/day)[a,k]			
	122.8 ‡ ± 1.8 § N=5[l]	116.7 * ± 2.0 N=4[l]	117.6 * ± 0.5 N=5[l]

(continued)

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

[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 animal 59 being found dead on the morning of postnatal day 27.
[d]Decrease in N is due to animal 16 being found dead on the morning of postnatal day 28.
[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 excluded because the animal had pulled feed into the cage and an accurate feed weight could not be obtained.
[g]Decrease in N is due to animal 46 being found dead after dosing on postnatal day 29.
[h]Decrease in N is due to animal 27 being found dead after dosing on postnatal day 30.
[i]Decrease in N is due to animal 87 being euthanized moribund after dosing on postnatal day 34.
[j]Decrease in N is due to animal 1 being found dead on the morning of postnatal day 40.
[k]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
[l]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.
‡$p<0.05$; 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-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole-Treated F_1 Females (page 1 of 7)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Females on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	7.7 ± 0.7 N=15	6.9 ± 0.8 N=15	5.9 ± 0.5 N=15
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	8.9 ± 0.4 N=15	8.8 ± 0.6 N=15	8.2 ± 0.5 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	10.5 ± 0.5 N=15	9.9 ± 0.5 N=15	9.0 ± 0.6 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
	11.6 ‡‡ ± 0.6 §§ N=15	10.9 ± 0.5 N=14[b]	9.0 ** ± 0.4 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	12.7 ± 0.5 § N=15	12.1 ± 0.5 N=14[b]	11.3 ± 0.4 N=14[b]
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	12.0 ± 0.5 N=15	12.5 ± 0.3 N=15	11.8 ± 0.3 N=15
Feed Consumption (pnd 27 to 28) (g/day)[a]			
	13.4 ‡ ± 0.3 § N=15	13.6 ± 0.3 N=15	12.3 ± 0.4 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	14.9 ‡‡ ± 0.5 §§ N=15	14.7 ± 0.3 N=14[b]	12.8 ** ± 0.5 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole-Treated F_1 Females (page 2 of 7)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 29 to 30) (g/day)[a]			
	13.5 ± 0.7 N=15	15.0 ± 0.4 N=13[b,c]	14.2 ± 0.5 N=15
Feed Consumption (pnd 30 to 31) (g/day)[a]			
	14.9 ‡‡‡ §§§ ± 0.5 N=15	14.3 ± 0.3 N=14[b]	12.3 *** ± 0.5 N=15
Feed Consumption (pnd 31 to 32) (g/day)[a]			
	15.5 ‡ §§ ± 0.4 N=15	15.1 ± 0.5 N=13[b]	13.5 * ± 0.6 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]			
	15.4 ‡ § ± 0.5 N=15	15.7 ± 0.4 N=13[b,c]	13.9 ± 0.5 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]			
#	16.5 ± 0.4 N=15	16.7 ± 0.5 N=13[b,c]	15.8 ± 0.8 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]			
	16.9 ± 0.6 N=15	16.0 ± 0.5 N=15	15.5 ± 0.9 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]			
	16.7 ‡‡ §§ ± 0.5 N=15	17.0 ± 0.5 N=15	14.3 ** ± 0.5 N=14[b]
Feed Consumption (pnd 36 to 37) (g/day)[a]			
#	17.5 ± 0.6 N=15	17.7 ± 0.4 N=15	17.2 ± 0.8 N=15
Feed Consumption (pnd 37 to 38) (g/day)[a]			
	18.2 ‡‡‡ §§§ ± 0.6 N=15	18.2 ± 0.5 N=15	15.0 *** ± 0.6 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole-Treated F_1 Females (page 3 of 7)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 38 to 39) (g/day)[a]	18.6 ‡ ± 0.6 N=15	19.5 ± 0.6 N=15	16.8 ± 0.9 N=15
Feed Consumption (pnd 39 to 40) (g/day)[a]	18.6 ± 0.5 N=14[d]	19.6 ± 0.5 N=14[c]	18.6 ± 0.7 N=15
Feed Consumption (pnd 40 to 41) (g/day)[a]	18.2 ‡ ± 0.4 § N=14	18.3 ± 0.5 N=15	16.2 * ± 0.7 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a]	18.5 ‡‡‡ ± 0.6 §§ N=14	18.9 ± 0.6 N=15	15.3 ** ± 0.6 N=15
Feed Consumption (pnd 42 to 43) (g/day)[a,e]	15.6 ‡ ± 0.2 N=5[b]	18.5 * ± 0.8 N=5	16.2 ± 0.7 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/day)[a]	15.2 ‡‡ ± 0.3 §§ N=14	15.2 ± 0.3 N=9[f]	13.6 ** ± 0.3 N=13[f]
Feed Consumption (pnd 22 to 43, treatment period) (g/day)[a,e]	15.1 ‡‡ ± 0.5 N=5[f]	16.0 ± 0.0 N=3[f]	13.3 * ± 0.3 N=4[f]
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	133.4 ± 12.1 § N=15	117.7 ± 13.8 N=15	101.1 ± 7.3 N=15

(continued)

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

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]			
	144.1 ± 5.5 N=15	140.8 ± 9.0 N=15	135.4 ± 9.4 N=15
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
	153.9 ± 7.3 N=15	144.9 ± 6.9 N=15	137.4 ± 9.1 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
	156.5 ‡ ± 7.8 §§ N=15	150.3 ± 6.7 N=14[b]	129.3 * ± 6.8 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	159.5 ± 6.0 N=15	154.5 ± 5.1 N=14[b]	150.3 ± 4.1 N=14[b]
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	140.6 ± 4.8 N=15	148.7 ± 2.4 N=15	148.5 ± 4.3 N=15
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
	147.4 ± 3.5 N=15	150.0 ± 2.1 N=15	143.8 ± 3.8 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	153.9 ‡ ± 4.4 § N=15	151.0 ± 2.3 N=14[b]	140.7 * ± 3.7 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
	129.9 ‡ ± 5.9 § N=15	147.5 * ± 3.7 N=13[b,c]	146.8 * ± 4.7 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	135.0 ‡ ± 4.3 § N=15	130.7 ± 2.5 N=14[b]	119.7 * ± 5.0 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole-Treated F_1 Females (page 5 of 7)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]	132.4 ± 2.6 N=15	130.1 ± 4.3 N=13[b]	123.3 ± 4.2 N=15
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]	124.1 ± 3.6 N=15	126.3 ± 2.6 N=13[b,c]	119.7 ± 3.1 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]	126.5 ± 2.1 N=15	128.7 ± 2.7 N=13[b,c]	128.4 ± 5.3 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]	122.6 ± 3.3 N=15	117.4 ± 3.7 N=15	120.6 ± 6.1 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]	116.8 ‡ ± 2.7 § N=15	118.3 ± 3.4 N=15	107.5 ± 3.2 N=14[b]
Feed Consumption (pnd 36 to 37) (g/kg/day)[a] #	117.1 ± 2.6 N=15	117.9 ± 2.0 N=15	121.6 ± 4.0 N=15
Feed Consumption (pnd 37 to 38) (g/kg/day)[a] #	116.6 † ± 2.9 Ÿ N=15	116.7 ± 1.7 N=15	103.7 Þ ± 4.6 N=15
Feed Consumption (pnd 38 to 39) (g/kg/day)[a] #	114.1 ± 2.6 N=15	120.2 ± 2.8 N=15	111.3 ± 4.4 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]	110.7 ± 2.2 § N=14[d]	115.9 ± 2.1 N=14[c]	118.9 ± 3.3 N=15

(continued)

Table 4-E. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Ketoconazole-Treated F_1 Females (page 6 of 7)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
#	104.9 ± 1.8 N=14	105.0 ± 2.2 N=15	100.7 ± 4.2 N=15
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
	103.5 ‡‡ ± 2.9 § N=14	105.7 ± 3.3 N=15	92.4 * ± 2.8 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[a,e]			
	86.9 ‡ ± 1.8 N=5[b]	99.5 ** ± 3.1 N=5	93.2 ± 2.3 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/kg/day)[a]			
	125.9 ‡‡ ± 1.3 § N=14	127.5 ± 0.6 N=9[f]	120.9 * ± 1.7 N=13[f]
Feed Consumption (pnd 22 to 43, treatment period) (g/kg/day)[a,e]			
	122.8 ‡‡ ± 1.8 § N=5[f]	125.3 ± 1.4 N=3[f]	114.6 * ± 1.5 N=4[f]

(continued)

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

[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 excluded because the animal had pulled feed into the cage and an accurate feed weight could not be obtained.
[d]Decrease in N is due to animal 1 being found dead on the morning of postnatal day 40.
[e]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
[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.
†$p<0.05$; Wald Chi-square Test for overall treatment effect in robust regression model.
Ÿ$p<0.05$; Linear trend test in robust regression model.
Þ$p<0.05$; 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 Propylthiouracil-Treated F_1 Females (page 1 of 7)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Females on Study	15	15	15
Feed Consumption (pnd 21 to 22) (g/day)[a]			
	7.7 ± 0.7 N=15	6.6 ± 1.0 N=13[b,c]	6.4 ± 0.4 N=14[b]
Feed Consumption (pnd 22 to 23) (g/day)[a]			
	8.9 ± 0.4 N=15	10.0 ± 0.8 N=15	8.7 ± 0.6 N=15
Feed Consumption (pnd 23 to 24) (g/day)[a]			
	10.5 ‡ ± 0.5 § N=15	10.3 ± 0.3 N=14[b]	9.1 * ± 0.4 N=15
Feed Consumption (pnd 24 to 25) (g/day)[a]			
#	11.6 ± 0.6 Ÿ N=15	10.8 ± 0.2 N=15	10.3 ± 0.3 N=15
Feed Consumption (pnd 25 to 26) (g/day)[a]			
	12.7 ± 0.5 N=15	12.4 ± 0.7 N=14[b]	13.1 ± 1.2 N=15
Feed Consumption (pnd 26 to 27) (g/day)[a]			
	12.0 ‡ ± 0.5 N=15	13.7 * ± 0.4 N=14[b]	11.5 ± 0.6 N=14[b]
Feed Consumption (pnd 27 to 28) (g/day)[a]			
#	13.4 ± 0.3 N=15	13.3 ± 0.5 N=15	14.3 ± 0.8 N=15
Feed Consumption (pnd 28 to 29) (g/day)[a]			
	14.9 ‡ ± 0.5 §§ N=15	15.0 ± 0.8 N=15	12.1 * ± 0.8 N=15

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil-Treated F_1 Females (page 2 of 7)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 29 to 30) (g/day)[a]			
	13.5 ± 0.7 N=15	14.5 ± 0.7 N=14[b]	13.7 ± 0.5 N=15
Feed Consumption (pnd 30 to 31) (g/day)[a]			
	14.9 ‡‡‡ ± 0.5 §§§ N=15	14.0 ± 0.5 N=14[c]	11.8 *** ± 0.5 N=15
Feed Consumption (pnd 31 to 32) (g/day)[a]			
	15.5 ‡‡‡ ± 0.4 §§§ N=15	14.3 ± 0.3 N=14[b]	12.5 *** ± 0.6 N=15
Feed Consumption (pnd 32 to 33) (g/day)[a]			
	15.4 ‡‡‡ ± 0.5 §§§ N=15	15.5 ± 0.4 N=15	12.5 *** ± 0.3 N=15
Feed Consumption (pnd 33 to 34) (g/day)[a]			
	16.5 ‡‡‡ ± 0.4 §§§ N=15	16.3 ± 0.5 N=15	12.1 *** ± 0.3 N=15
Feed Consumption (pnd 34 to 35) (g/day)[a]			
	16.9 ‡‡‡ ± 0.6 §§§ N=15	17.0 ± 0.5 N=15	11.7 *** ± 0.5 N=15
Feed Consumption (pnd 35 to 36) (g/day)[a]			
	16.7 ‡‡‡ ± 0.5 §§§ N=15	17.1 ± 0.8 N=15	10.3 *** ± 0.5 N=15
Feed Consumption (pnd 36 to 37) (g/day)[a]			
	17.5 ‡‡‡ ± 0.6 §§§ N=15	17.3 ± 0.9 N=14[d]	11.6 *** ± 0.7 N=14[b]
Feed Consumption (pnd 37 to 38) (g/day)[a]			
	18.2 ‡‡‡ ± 0.6 §§§ N=15	15.9 * ± 0.7 N=14[b]	9.9 *** ± 0.5 N=14[c]

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil-Treated F_1 Females (page 3 of 7)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 38 to 39) (g/day)[a]	18.6 ‡‡‡ ± 0.6 §§§ N=15	18.1 ± 0.7 N=15	10.3 *** ± 0.4 N=15
Feed Consumption (pnd 39 to 40) (g/day)[a]	18.6 ‡‡‡ ± 0.5 §§§ N=14[e]	18.9 ± 0.6 N=15	10.7 *** ± 0.5 N=15
Feed Consumption (pnd 40 to 41) (g/day)[a]	18.2 ‡‡‡ ± 0.4 §§§ N=14	17.7 ± 0.6 N=15	10.3 *** ± 0.6 N=15
Feed Consumption (pnd 41 to 42) (g/day)[a]	18.5 ‡‡‡ ± 0.6 §§§ N=14	16.9 ± 0.5 N=15	8.5 *** ± 0.4 N=15
Feed Consumption (pnd 42 to 43) (g/day)[a,f]	15.6 ‡‡‡ ± 0.2 §§§ N=5[b]	19.9 ± 2.2 N=5	8.5 ** ± 0.7 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/day)[a]	15.2 ‡‡‡ ± 0.3 §§§ N=14	14.6 ± 0.2 N=10[g]	11.2 *** ± 0.3 N=13[g]
Feed Consumption (pnd 22 to 43, treatment period) (g/day)[a,f]	15.1 ‡‡ ± 0.5 §§§ N=5[g]	14.7 ± 0.5 N=3[g]	11.2 ** ± 0.5 N=3[g]
Feed Consumption (pnd 21 to 22) (g/kg/day)[a]	133.4 ± 12.1 N=15	113.8 ± 15.3 N=13[b,c]	109.9 ± 7.6 N=14[b]

(continued)

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

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 22 to 23) (g/kg/day)[a]			
	144.1 ± 5.5 N=15	161.1 ± 12.3 N=15	140.0 ± 8.6 N=15
Feed Consumption (pnd 23 to 24) (g/kg/day)[a]			
	153.9 ‡ ± 7.3 §§ N=15	153.1 ± 3.6 N=14[b]	133.8 * ± 5.7 N=15
Feed Consumption (pnd 24 to 25) (g/kg/day)[a]			
#	156.5 ± 7.8 Ÿ N=15	148.2 ± 2.2 N=15	140.3 ± 3.7 N=15
Feed Consumption (pnd 25 to 26) (g/kg/day)[a]			
	159.5 ± 6.0 N=15	157.7 ± 8.4 N=14[b]	165.0 ± 14.4 N=15
Feed Consumption (pnd 26 to 27) (g/kg/day)[a]			
	140.6 ‡‡ ± 4.8 N=15	162.9 * ± 5.3 N=14[b]	135.4 ± 7.2 N=14[b]
Feed Consumption (pnd 27 to 28) (g/kg/day)[a]			
#	147.4 ± 3.5 N=15	147.1 ± 5.1 N=15	157.6 ± 9.0 N=15
Feed Consumption (pnd 28 to 29) (g/kg/day)[a]			
	153.9 ‡ ± 4.4 §§ N=15	156.6 ± 8.7 N=15	126.2 * ± 8.4 N=15
Feed Consumption (pnd 29 to 30) (g/kg/day)[a]			
	129.9 ± 5.9 N=15	141.7 ± 6.2 N=14[b]	134.8 ± 4.7 N=15
Feed Consumption (pnd 30 to 31) (g/kg/day)[a]			
	135.0 ‡‡‡ ± 4.3 §§§ N=15	128.7 ± 3.8 N=14[c]	110.4 *** ± 4.5 N=15

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil-Treated F_1 Females (page 5 of 7)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 31 to 32) (g/kg/day)[a]			
	132.4 ‡‡‡ ± 2.6 §§§ N=15	124.2 ± 2.1 N=14[b]	112.3 *** ± 4.6 N=15
Feed Consumption (pnd 32 to 33) (g/kg/day)[a]			
	124.1 ‡‡‡ ± 3.6 §§§ N=15	126.5 ± 1.8 N=15	107.6 *** ± 2.2 N=15
Feed Consumption (pnd 33 to 34) (g/kg/day)[a]			
	126.5 ‡‡‡ ± 2.1 §§§ N=15	126.4 ± 3.6 N=15	101.8 *** ± 3.0 N=15
Feed Consumption (pnd 34 to 35) (g/kg/day)[a]			
	122.6 ‡‡‡ ± 3.3 §§§ N=15	125.7 ± 2.7 N=15	95.9 *** ± 3.7 N=15
Feed Consumption (pnd 35 to 36) (g/kg/day)[a]			
	116.8 ‡‡‡ ± 2.7 §§§ N=15	121.2 ± 5.5 N=15	82.2 *** ± 3.4 N=15
Feed Consumption (pnd 36 to 37) (g/kg/day)[a]			
	117.1 ‡‡‡ ± 2.6 §§§ N=15	119.0 ± 5.6 N=14[d]	92.9 ** ± 5.3 N=14[b]
Feed Consumption (pnd 37 to 38) (g/kg/day)[a]			
	116.6 ‡‡‡ ± 2.9 §§§ N=15	102.5 * ± 4.1 N=13[b,d]	78.4 *** ± 3.9 N=14[c]
Feed Consumption (pnd 38 to 39) (g/kg/day)[a]			
	114.1 ‡‡‡ ± 2.6 §§§ N=15	115.1 ± 4.0 N=15	80.6 *** ± 2.7 N=15
Feed Consumption (pnd 39 to 40) (g/kg/day)[a]			
	110.7 ‡‡‡ ± 2.2 §§§ N=14[e]	115.6 ± 2.4 N=15	82.2 *** ± 3.5 N=15

(continued)

Table 4-F. Summary and Statistical Analysis of the Feed Consumption During the Post Wean Period for the Propylthiouracil-Treated F_1 Females (page 6 of 7)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Feed Consumption (pnd 40 to 41) (g/kg/day)[a]			
	104.9 ‡‡‡ ± 1.8 §§§ N=14	104.3 ± 2.6 N=15	78.4 *** ± 4.0 N=15
Feed Consumption (pnd 41 to 42) (g/kg/day)[a]			
	103.5 ‡‡‡ ± 2.9 §§§ N=14	97.1 ± 2.0 N=15	64.7 *** ± 2.4 N=15
Feed Consumption (pnd 42 to 43) (g/kg/day)[a,f]			
	86.9 ‡‡ ± 1.8 §§ N=5[b]	111.6 ± 12.3 N=5	62.9 ± 3.9 N=5
Feed Consumption (pnd 22 to 42, treatment period) (g/kg/day)[a]			
	125.9 ‡‡‡ ± 1.3 §§§ N=14	124.7 ± 1.7 N=10[g]	106.6 *** ± 1.7 N=13[g]
Feed Consumption (pnd 22 to 43, treatment period) (g/kg/day)[a,f]			
	122.8 ‡‡‡ ± 1.8 §§§ N=5[g]	121.4 ± 3.0 N=3[g]	102.5 *** ± 2.3 N=3[g]

(continued)

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

[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]Decrase in N is due to animal 101 being found outside of it's cage on the morning of postnatal day 37 and therefore the body weight on postnatal day 37 and the feed consumption value for postnatal days 36-37 were excluded.
[e]Decrease in N is due to animal 1 being found dead on the morning of postnatal day 40.
[f]Includes those animals that were not scheduled for sacrifice until postnatal day 43.
[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.
[Ÿ]$p<0.05$; Linear trend test in robust regression model.

Table 5-A. Summary of Clinical Observations During the Post Wean Period for the Atrazine-Treated F_1 Females (page 1 of 2)

A. Clinical Observations Summarized by Group

	Atrazine (mg/kg/day, po)		
Observation	0	75	150
Rooting: post dosing		1	4
Salivation: prior to dosing		6	9
Sore(s)		1	1

B. Clinical Observations Summarized by Group and Day

		Atrazine (mg/kg/day, po)		
Day[a]	Observation[b]	0	75	150
29	Salivation: prior to dosing			2
30	Salivation: prior to dosing			3
	Sore(s): neck			1
31	Salivation: prior to dosing		2	2
	Sore(s): neck			1
32	Salivation: prior to dosing		1	1
	Sore(s): neck			1
34	Salivation: prior to dosing		1	
35	Salivation: prior to dosing			1
36	Salivation: prior to dosing			2
37	Salivation: prior to dosing		2	2
38	Rooting: post dosing			1
	Salivation: prior to dosing		1	3
	Sore(s): neck, treated with 0.2% nitrofurazone			1
39	Rooting: post dosing			1
	Salivation: prior to dosing		2	5
	Sore(s): head		1	
	neck			1
40	Rooting: post dosing			2
	Salivation: prior to dosing		2	3
	Sore(s): head		1	
	neck			1
41	Rooting: post dosing		1	1
	Salivation: prior to dosing		4	7
	Sore(s): head, healing		1	
	neck, treated with 0.2% nitrofurazone			1

(continued)

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

B. Clinical Observations Summarized by Group and Day

Day[a]	Observation[b]	Atrazine (mg/kg/day, po) 0	75	150
42	Rooting: post dosing			1
	Salivation: prior to dosing		1	3
	Sore(s): neck, treated with 0.2% nitrofurazone			1
43	Sore(s): neck			1

[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 Fenarimol-Treated F_1 Females (page 1 of 2)

A. Clinical Observations Summarized by Group

	Fenarimol (mg/kg/day, po)		
Observation	0	50	250
No water bottle on cage at time of dosing		1	
Rooting: post dosing		6	5
Salivation: prior to dosing		4	7
Sore(s)			2

B. Clinical Observations Summarized by Group and Day

		Fenarimol (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	250
29	Salivation: prior to dosing			1
30	Salivation: prior to dosing			1
31	Salivation: prior to dosing			3
32	No water bottle on cage at time of dosing		1	
	Salivation: prior to dosing		1	
33	Salivation: prior to dosing		2	1
34	Salivation: prior to dosing		1	1
35	Salivation: prior to dosing		1	1
36	Salivation: prior to dosing		1	1
37	Salivation: prior to dosing		1	3
38	Rooting: post dosing			1
	Salivation: prior to dosing		1	3
	Sore(s): head			1
39	Rooting: post dosing		1	1
	Salivation: prior to dosing		1	3
	Sore(s): head			1
40	Rooting: post dosing		1	1
	Salivation: prior to dosing		1	5
	Sore(s): head			1
41	Rooting: post dosing		3	4
	Salivation: prior to dosing		1	7
	Sore(s): head, healing			1

(continued)

Table 5-B. Summary of Clinical Observations During the Post Wean Period for the Fenarimol-Treated F_1 Females (page 2 of 2)

B. Clinical Observations Summarized by Group and Day

Day[a]	Observation[b]	Fenarimol (mg/kg/day, po) 0	50	250
42	Rooting: post dosing		2	
	Salivation: prior to dosing		1	1
	Sore(s): shoulder(s)			1
43	Sore(s): shoulder(s)			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 Methoxychlor-Treated F_1 Females (page 1 of 1)

A. Clinical Observations Summarized by Group

	Methoxychlor (mg/kg/day, po)		
Observation	0	25	50
Found dead		1	
Rooting: post dosing			1
Salivation: prior to dosing		1	3

B. Clinical Observations Summarized by Group and Day

		Methoxychlor (mg/kg/day, po)		
Day[a]	Observation[b]	0	25	50
37	Salivation: prior to dosing			2
38	Found dead in the afternoon		1	
	Salivation: prior to dosing			1
39	Salivation: prior to dosing		1	
41	Rooting: post dosing			1
42	Rooting: post 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 Bisphenol A-Treated F_1 Females (page 1 of 2)

A. Clinical Observations Summarized by Group

	Bisphenol A (mg/kg/day, po)		
Observation	0	400	600
Efflux of the dosing solution/suspension		1	2
Euthanized moribund		1	
Found dead	1	3	1
Gasping		1	
Piloerection			1
Respiration: audible			2
Rooting: post dosing		7	15
Salivation: prior to dosing		12	10

B. Clinical Observations Summarized by Group and Day

		Bisphenol A (mg/kg/day, po)		
Day[a]	Observation[b]	0	400	600
22	Efflux of the dosing solution/suspension			1
23	Rooting: post dosing			1
24	Rooting: post dosing		1	1
25	Rooting: post dosing		1	
26	Rooting: post dosing		2	2
27	Found dead in the morning		1	
	Piloerection			1
	Rooting: post dosing		4	2
	Salivation: prior to dosing		2	1
28	Found dead in the morning		1	
	Rooting: post dosing		4	11
	Salivation: prior to dosing		2	2
29	Found dead after dosing			1
	Respiration: audible			1
	Rooting: post dosing			4
	Salivation: prior to dosing		1	2
30	Found dead after dosing		1	
	Rooting: post dosing			2
	Salivation: prior to dosing		2	
31	Salivation: prior to dosing			1
33	Salivation: prior to dosing		2	2

(continued)

Table 5-D. Summary of Clinical Observations During the Post Wean Period for the Bisphenol A-Treated F_1 Females (page 2 of 2)

B. Clinical Observations Summarized by Group and Day

		Bisphenol A (mg/kg/day, po)		
Day[a]	Observation[b]	0	400	600
34	Euthanized moribund after dosing		1	
	Gasping		1	
	Rooting: post dosing		2	3
	Salivation: prior to dosing		6	4
35	Efflux of the dosing solution/suspension			1
	Rooting: post dosing		1	2
	Salivation: prior to dosing		6	5
36	Efflux of the dosing solution/suspension		1	
	Respiration: audible			1
	Rooting: post dosing		1	
	Salivation: prior to dosing		3	4
37	Rooting: post dosing		2	1
	Salivation: prior to dosing		4	3
38	Rooting: post dosing		1	1
	Salivation: prior to dosing		3	1
39	Rooting: post dosing		1	3
	Salivation: prior to dosing		4	4
40	Found dead in the morning	1		
	Rooting: post dosing			3
	Salivation: prior to dosing		3	5
41	Rooting: post dosing		2	1
	Salivation: prior to dosing		4	5
42	Rooting: post dosing		1	
	Salivation: prior to dosing		2	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 Ketoconazole-Treated F_1 Females (page 1 of 1)

A. Clinical Observations Summarized by Group

	Ketoconazole (mg/kg/day, po)		
Observation	0	50	100
Efflux of the dosing solution/suspension			1
Found dead	1		
Piloerection		1	
Rooting: post dosing		3	5
Salivation: prior to dosing		6	6

B. Clinical Observations Summarized by Group and Day

		Ketoconazole (mg/kg/day, po)		
Day[a]	Observation[b]	0	50	100
27	Piloerection		1	
28	Salivation: prior to dosing			1
29	Salivation: prior to dosing			1
30	Rooting: post dosing		1	
	Salivation: prior to dosing			1
33	Salivation: prior to dosing			2
34	Rooting: post dosing		1	
	Salivation: prior to dosing		1	2
35	Salivation: prior to dosing		3	2
36	Rooting: post dosing		1	
	Salivation: prior to dosing		2	1
37	Efflux of the dosing solution/suspension			1
	Rooting: post dosing		1	4
	Salivation: prior to dosing		3	2
38	Rooting: post dosing			1
	Salivation: prior to dosing		2	1
39	Rooting: post dosing		2	1
	Salivation: prior to dosing		1	2
40	Found dead in the morning	1		
	Salivation: prior to dosing		3	2
41	Rooting: post dosing			2
	Salivation: prior to dosing		3	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 Propylthiouracil-Treated F_1 Females (page 1 of 1)

A. Clinical Observations Summarized by Group

	Propylthiouracil (mg/kg/day, po)		
Observation	0	2	25
Animal found outside of the cage at time of dosing		1	
Found dead	1		
Piloerection			1
Rooting: post dosing		3	5
Salivation: prior to dosing			6

B. Clinical Observations Summarized by Group and Day

		Propylthiouracil (mg/kg/day, po)		
Day[a]	Observation[b]	0	2	25
27	Rooting: post dosing			1
28	Rooting: post dosing			2
33	Salivation: prior to dosing			1
34	Rooting: post dosing		1	1
	Salivation: prior to dosing			1
35	Salivation: prior to dosing			2
37	Animal found outside of the cage at time of dosing		1	
	Rooting: post dosing		2	1
	Salivation: prior to dosing			1
38	Rooting: post dosing			2
39	Salivation: prior to dosing			1
40	Found dead in the morning	1		
	Piloerection			1
	Salivation: prior to dosing			3
41	Salivation: prior to dosing			2
42	Salivation: prior to dosing			1

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

Table 6-A. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Atrazine-Treated F_1 Females (page 1 of 3)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Females on Study	15	15	15
Number of Females Evaluated	15	15	15[a]
Average Postnatal Day of Vaginal Opening[b]	32.9 ‡‡‡ ± 0.4 §§§ N=15	34.2 ± 0.4 N=15	36.4 *** ± 0.6 N=15
Average Body Weight (g) on Day of Acquisition[b]	127.89 ± 3.20 N=15	128.07 ± 3.03 N=15	129.81 ± 2.91 N=15
Average Number of Days Since Vaginal Opening till First Estrus[b]	1.1 ± 0.4 N=15	1.1 ± 0.5 N=15	1.0 ± 0.5 N=15
Average Postnatal Day of First Estrus[b]	34.1 ‡‡ ± 0.4 §§§ N=15	35.3 ± 0.8 N=15	37.4 ** ± 0.7 N=15
Number of Females Cycling	15	15	10
Percent of Females Cycling	100.00	100.00	90.91
Average Number of Days Since Vaginal Opening till Start of First Cycle[b]	0.1 ± 0.1 N=15	0.5 ± 0.2 N=15	0.3 ± 0.2 N=10
Average Postnatal Day of Start of First Cycle[b]	33.0 ‡‡ ± 0.4 §§§ N=15	34.7 * ± 0.5 N=15	35.7 ** ± 0.6 N=10

(continued)

Table 6-A. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Atrazine-Treated F_1 Females (page 2 of 3)

	Atrazine (mg/kg/day, po)		
	0	75	150
Average Number of Days Since Vaginal Opening till End of First Cycle[b]			
	4.5 ± 0.3 N=15	3.8 ± 0.2 N=15	4.1 ± 0.1 N=10
Average Postnatal Day of End of First Cycle[b]			
	37.4 ‡ ± 0.5 §§ N=15	38.0 ± 0.5 N=15	39.5 * ± 0.5 N=10
Average Number of Days in Diestrus During the First Cycle[b]			
	1.4 ‡ ± 0.2 N=15	0.7 * ± 0.1 N=15	1.3 ± 0.2 N=10
Average Number of Days in Proestrus During the First Cycle[b]			
	1.1 ± 0.2 N=15	0.9 ± 0.1 N=15	1.0 ± 0.0 N=10
Average Number of Days in Estrus During the First Cycle[b]			
	1.3 ± 0.1 N=15	1.2 ± 0.1 N=15	1.1 ± 0.1 N=10
Average Number of Days in Metestrus During the First Cycle[b]			
	1.7 ± 0.2 N=15	1.4 ± 0.1 N=15	1.5 ± 0.2 N=10
Number of Females with Prolonged Estrus			
	0	2	0
Percent of Females with Prolonged Estrus			
	0.00	13.33	0.00
Number of Females with Prolonged Diestrus			
	0	0	0
Percent of Females with Prolonged Diestrus			
	0.00	0.00	0.00

(continued)

Table 6-A. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Atrazine-Treated F_1 Females (page 3 of 3)

[a]Animals 12, 17, 31 and 79 were only evaluated for first day of estrus since there were not enough vaginal smears to evaluate any of the other endpoints.
[b]Reported as the mean ± S.E.M.; pnd = postnatal day.
[c]Reported as the adjusted mean ± S.E.M. (body weight at acquisition 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.

Table 6-B. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Fenarimol-Treated F_1 Females (page 1 of 3)

	Fenarimol (mg/kg/day, po)		
	0	50	250
No. of Females on Study	15	15	15
Number of Females Evaluated	15	15	15[a]
Average Postnatal Day of Vaginal Opening[b]			
#	32.9 ± 0.4 N=15	33.7 ± 0.4 N=15	34.2 ± 0.7 N=15
Average Body Weight (g) on Day of Acquisition[b]			
#	127.89 †† ± 3.20 ŸŸ N=15	132.62 ± 2.45 N=15	114.53 Þ ± 4.35 N=15
Average Number of Days Since Vaginal Opening till First Estrus[b]			
	1.1 ± 0.4 N=15	1.1 ± 0.5 N=15	1.5 ± 0.5 N=15
Average Postnatal Day of First Estrus[b]			
	34.1 ± 0.4 N=15	34.7 ± 0.8 N=15	35.7 ± 0.9 N=15
Number of Females Cycling	15	13	13
Percent of Females Cycling	100.00	86.67	100.00
Average Number of Days Since Vaginal Opening till Start of First Cycle[b]			
#	0.1 † ± 0.1 N=15	0.9 Þ ± 0.4 N=13	0.5 ± 0.2 N=13
Average Postnatal Day of Start of First Cycle[b]			
	33.0 ± 0.4 N=15	34.5 ± 0.5 N=13	34.3 ± 0.7 N=13

(continued)

Table 6-B. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Fenarimol-Treated F_1 Females (page 2 of 3)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Average Number of Days Since Vaginal Opening till End of First Cycle[b]			
	4.5 ± 0.3 N=15	4.2 ± 0.5 N=13	3.8 ± 0.5 N=13
Average Postnatal Day of End of First Cycle[b]			
	37.4 ± 0.5 N=15	37.7 ± 0.6 N=13	37.6 ± 0.6 N=13
Average Number of Days in Diestrus During First Cycle[b]			
	1.4 ± 0.2 N=15	1.0 ± 0.1 N=13	1.1 ± 0.1 N=13
Average Number of Days in Proestrus During First Cycle[b]			
	1.1 ‡ ± 0.2 § N=15	0.9 ± 0.1 N=13	0.6 * ± 0.1 N=13
Average Number of Days in Estrus During First Cycle[b]			
	1.3 ± 0.1 N=15	0.9 ± 0.1 N=13	1.3 ± 0.4 N=13
Average Number of Days in Metestrus During First Cycle[b]			
	1.7 ± 0.2 N=15	1.4 ± 0.2 N=13	1.2 ± 0.2 N=13
Number of Females with Prolonged Estrus			
	0	0	2
Percent of Females with Prolonged Estrus			
	0.00	0.00	15.38
Number of Females with Prolonged Diestrus			
	0	0	0
Percent of Females with Prolonged Diestrus			
	0.00	0.00	0.00

(continued)

Table 6-B. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Fenarimol-Treated F_1 Females (page 3 of 3)

[a]Animals 5 and 44 were only evaluated for first day of estrus since there were not enough vaginal smears to evaluate any of the other endpoints.
[b]Reported as the mean ± S.E.M.; pnd = postnatal day.
[c]Reported as the adjusted mean ± S.E.M. (body weight at acquisition 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.
[†]$p<0.05$; 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.
[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.
[‡]$p<0.05$; ANOVA Test.
[§]$p<0.05$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.

Table 6-C. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Methoxychlor-Treated F_1 Females (page 1 of 3)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Females on Study	15	15	15
Number of Females Evaluated	15	15	15
Average Postnatal Day of Vaginal Opening[a]			
#	32.9 †††	29.8 **ÞÞÞ**	27.4 **ÞÞÞ**
	± 0.4 **ŸŸŸ**	± 0.6	± 0.3
	N=15	N=15	N=15
Average Body Weight (g) on Day of Acquisition[a]			
	127.89 ‡‡‡	104.85 ***	89.54 ***
	± 3.20 **§§§**	± 4.13	± 2.40
	N=15	N=15	N=15
Average Days Since Vaginal Opening till First Estrus[a]			
#	1.1	0.6	0.9
	± 0.4	± 0.2	± 0.3
	N=15	N=15	N=15
Average Postnatal Day of First Estrus[a]			
	34.1 ‡‡‡	30.4 ***	28.3 ***
	± 0.4 **§§§**	± 0.5	± 0.5
	N=15	N=15	N=15
Number of Females Cycling	15	14	15
Percent of Females Cycling	100.00	93.33	100.00
Average Number of Days Since Vaginal Opening till Start of First Cycle[a]			
	0.1	1.5	1.4
	± 0.1 **§**	± 0.7	± 0.4
	N=15	N=14	N=15
Average Postnatal Day of Start of First Cycle[a]			
	33.0 ‡‡‡	31.5	28.8 ***
	± 0.4 **§§§**	± 0.7	± 0.4
	N=15	N=14	N=15

(continued)

Table 6-C. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Methoxychlor-Treated F_1 Females (page 2 of 3)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Average Number of Days Since Vaginal Opening till End of First Cycle[a]			
	4.5 ± 0.3 N=15	5.4 ± 0.8 N=14	4.9 ± 0.5 N=15
Average Postnatal Day of End of First Cycle[a]			
	37.4 ‡‡‡ ± 0.5 §§§ N=15	35.4 * ± 0.7 N=14	32.3 *** ± 0.5 N=15
Average Number of Days in Diestrus During First Cycle[a]			
	1.4 ± 0.2 § N=15	1.3 ± 0.2 N=14	0.9 ± 0.1 N=15
Average Number of Days in Proestrus During First Cycle[a]			
	1.1 ± 0.2 N=15	1.0 ± 0.2 N=14	1.2 ± 0.1 N=15
Average Number of Days in Estrus During First Cycle[a]			
	1.3 ± 0.1 N=15	1.3 ± 0.1 N=14	1.3 ± 0.2 N=15
Average Number of Days in Metestrus During First Cycle[a]			
	1.7 ± 0.2 § N=15	1.2 ± 0.1 N=14	1.2 ± 0.2 N=15
Number of Females with Prolonged Estrus			
	0	7	5
Percent of Females with Prolonged Estrus			
	0.00 £	46.67 ǂǂ	33.33 ǂǂ
Number of Females with Prolonged Diestrus			
	0	0	0
Percent of Females with Prolonged Diestrus			
	0.00	0.00	0.00

(continued)

Table 6-C. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Methoxychlor-Treated F_1 Females (page 3 of 3)

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Reported as the adjusted mean ± S.E.M. (body weight at acquisition 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.
ŧŧŧ$p<0.001$; 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.
‡‡‡$p<0.001$; 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.
£$p<0.05$; Chi-Square Test.
##$p<0.01$; Fishers' Exact Test.

Table 6-D. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Bisphenol A-Treated F_1 Females (page 1 of 3)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
No. of Females on Study	15	15	15
Number of Females Evaluated	15	12[a]	14[b]
Average Postnatal Day of Vaginal Opening[c]	32.3 ± 0.4 N=15	33.0 ± 0.6 N=12	32.3 ± 0.7 N=14
Average Body Weight (g) on Day of Acquisition[c]	122.70 ‡ ± 3.17 §§ N=15	116.36 ± 3.50 N=12	108.42 * ± 3.96 N=14
Average Number of Days Since Vaginal Opening till First Estrus[c]	1.2 ± 0.5 N=15	1.4 ± 0.5 N=12	2.0 ± 0.7 N=14
Average Postnatal Day of First Estrus[c]	33.5 ± 0.8 N=15	34.4 ± 1.0 N=12	34.3 ± 1.1 N=14
Number of Females Cycling	14	11	11
Percent of Females Cycling	93.33	100.00	78.57
Average Number of Days Since Vaginal Opening till Start of First Cycle[c]			
#	0.9 ± 0.3 N=14	0.8 ± 0.4 N=11	2.0 ± 0.8 N=11
Average Postnatal Day of Start of First Cycle[c]	33.1 ± 0.6 N=14	33.9 ± 0.9 N=11	33.7 ± 1.0 N=11

(continued)

Table 6-D. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Bisphenol A-Treated F_1 Females (page 2 of 3)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Average Number of Days Since Vaginal Opening till End of First Cycle[c]			
	5.0 ± 0.6 N=14	4.0 ± 0.5 N=11	5.0 ± 0.8 N=11
Average Postnatal Day of End of First Cycle[c]			
#	37.3 ± 0.7 N=14	37.1 ± 0.7 N=11	36.7 ± 1.1 N=11
Average Number of Days in Diestrus During First Cycle[c]			
	2.0 ± 0.4 N=14	1.5 ± 0.2 N=11	1.4 ± 0.3 N=11
Average Number of Days in Proestrus During First Cycle[c]			
	0.5 ± 0.2 N=14	0.5 ± 0.2 N=11	0.2 ± 0.1 N=11
Average Number of Days in Estrus During First Cycle[c]			
	1.1 ± 0.1 N=14	1.2 ± 0.1 N=11	1.2 ± 0.2 N=11
Average Number of Days in Metestrus During First Cycle[c]			
	1.6 ± 0.3 N=14	1.0 ± 0.0 N=11	1.2 ± 0.2 N=11
Number of Females with Prolonged Estrus			
	1	1	3
Percent of Females with Prolonged Estrus			
	6.67	9.09	21.43
Number of Females with Prolonged Diestrus			
	1	3	2
Percent of Females with Prolonged Diestrus			
	6.67	27.27	14.29

(continued)

Table 6-D. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Bisphenol A-Treated F_1 Females (page 3 of 3)

[a]Animal 16 was found dead on the morning of postnatal day 28; animal 27 was found dead after dosing on postnatal day 30; animal 59 was found dead on the morning of postnatal day 27 and animal 87 was only evaluated for first day of estrus since there were not enough vaginal smears to evaluate any of the other endpoints.
[b]Animal 46 was found dead after dosing on postnatal day 29.
[c]Reported as the mean $\pm$ S.E.M.; pnd = postnatal day.
[d]Reported as the adjusted mean $\pm$ S.E.M. (body weight at acquisition 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.
[§§]$p<0.01$; Test for Linear Trend.
[*]$p<0.05$; Dunnett's Test.

Table 6-E. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Ketoconazole-Treated F_1 Females (page 1 of 3)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Females on Study	15	15	15
Number of Females Evaluated	15	15	15[a]
Average Postnatal Day of Vaginal Opening[b]	32.3 ± 0.4 N=15	33.0 ± 0.4 N=15	33.7 ± 0.6 N=15
Average Body Weight (g) on Day of Acquisition[b]	122.70 ± 3.17 N=15	126.54 ± 2.54 N=15	122.60 ± 3.65 N=15
Average Number of Days Since Vaginal Opening till First Estrus[b]	1.2 ± 0.5 N=15	0.3 ± 0.2 N=15	1.4 ± 0.5 N=15
Average Postnatal Day of First Estrus[b]	33.5 ± 0.8 N=15	33.3 ± 0.6 N=15	35.1 ± 0.8 N=15
Number of Females Cycling	14	13	11
Percent of Females Cycling	93.33	86.67	84.62
Average Number of Days Since Vaginal Opening till Start of First Cycle[b]	0.9 ± 0.3 N=14	1.4 ± 0.4 N=13	1.1 ± 0.3 N=11
Average Postnatal Day of Start of First Cycle[b]	33.1 ± 0.6 N=14	34.3 ± 0.6 N=13	33.9 ± 0.6 N=11

(continued)

Table 6-E. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Ketoconazole-Treated F_1 Females (page 2 of 3)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Average Number of Days Since Vaginal Opening till End of First Cycle[b]			
	5.0 ± 0.6 N=14	5.5 ± 0.5 N=13	4.6 ± 0.6 N=11
Average Postnatal Day of End of First Cycle[b]			
	37.3 ± 0.7 N=14	38.5 ± 0.5 N=13	37.5 ± 0.8 N=11
Average Number of Days in Diestrus During First Cycle[b]			
	2.0 ± 0.4 N=14	1.8 ± 0.4 N=13	1.5 ± 0.2 N=11
Average Number of Days in Proestrus During First Cycle[b]			
	0.5 ± 0.2 N=14	0.4 ± 0.1 N=13	0.2 ± 0.1 N=11
Average Number of Days in Estrus During First Cycle[b]			
#	1.1 † ± 0.1 Ÿ N=14	1.5 ± 0.2 N=13	1.5 Þ ± 0.2 N=11
Average Number of Days in Metestrus During First Cycle[b]			
	1.6 ± 0.3 N=14	1.4 ± 0.2 N=13	1.2 ± 0.2 N=11
Number of Females with Prolonged Estrus			
	1	5	3
Percent of Females with Prolonged Estrus			
	6.67	33.33	23.08
Number of Females with Prolonged Diestrus			
	1	1	0
Percent of Females with Prolonged Diestrus			
	6.67	6.67	0.00

(continued)

Table 6-E. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Ketoconazole-Treated F_1 Females (page 3 of 3)

[a]Animals 19 and 24 were only evaluated for first day of estrus since there were not enough vaginal smears to evaluate any of the other endpoints.
[b]Reported as the mean ± S.E.M.; pnd = postnatal day.
[c]Reported as the adjusted mean ± S.E.M. (body weight at acquisition 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.
[†]$p<0.05$; Wald Chi-square Test for overall treatment effect in robust regression model.
[Ÿ]$p<0.05$; Linear trend test in robust regression model.
[Þ]$p<0.05$; Individual t-test for pairwise comparisons to control in robust regression model.

Table 6-F. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Propylthiouracil-Treated F_1 Females (page 1 of 3)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Females on Study	15	15	15
Number of Females Evaluated	15	15	15
Average Postnatal Day of Vaginal Opening[a]	32.3 ± 0.4 N=15	33.3 ± 0.5 N=15	33.1 ± 0.4 N=15
Average Body Weight (g) on Day of Acquisition[a]	122.70 ‡ ± 3.17 § N=15	127.35 ± 2.53 N=15	117.71 ± 1.86 N=15
Average Number of Days Since Vaginal Opening till First Estrus[a]	1.2 ± 0.5 N=15	0.3 ± 0.3 N=14	0.7 ± 0.3 N=15
Average Postnatal Day of First Estrus[a]			
#	33.5 ± 0.8 N=15	33.6 ± 0.5 N=14	33.8 ± 0.5 N=15
Number of Females Cycling	14	10	14
Percent of Females Cycling	93.33	66.67	93.33
Average Number of Days Since Vaginal Opening till Start of First Cycle[a]	0.9 ± 0.3 N=14	1.8 ± 0.6 N=10	0.7 ± 0.4 N=14
Average Postnatal Day of Start of First Cycle[a]	33.1 ± 0.6 N=14	35.0 ± 0.7 N=10	33.6 ± 0.4 N=14

(continued)

Table 6-F. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Propylthiouracil-Treated F_1 Females (page 2 of 3)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Average Number of Days Since Vaginal Opening till End of First Cycle[a]			
	5.0 ± 0.6 N=14	5.8 ± 0.6 N=10	4.2 ± 0.5 N=14
Average Postnatal Day of End of First Cycle[a]			
	37.3 ± 0.7 N=14	39.0 ± 0.6 N=10	37.1 ± 0.6 N=14
Average Number of Days in Diestrus During First Cycle[a]			
	2.0 ± 0.4 N=14	1.4 ± 0.3 N=10	1.4 ± 0.3 N=14
Average Number of Days in Proestrus During First Cycle[a]			
	0.5 ± 0.2 N=14	0.6 ± 0.2 N=10	0.4 ± 0.1 N=14
Average Number of Days in Estrus During First Cycle[a]			
	1.1 ± 0.1 N=14	1.3 ± 0.2 N=10	1.3 ± 0.1 N=14
Average Number of Days in Metestrus During First Cycle[a]			
	1.6 ± 0.3 N=14	1.7 ± 0.4 N=10	1.4 ± 0.2 N=14
Number of Females with Prolonged Estrus			
	1	1	1
Percent of Females with Prolonged Estrus			
	6.67	6.67	6.67
Number of Females with Prolonged Diestrus			
	1	4	0
Percent of Females with Prolonged Diestrus			
	6.67	26.67	0.00

(continued)

Table 6-F. Summary and Statistical Analysis of the Vaginal Opening and Vaginal Cytology for the Propylthiouracil-Treated F_1 Females (page 3 of 3)

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Reported as the adjusted mean ± S.E.M. (body weight at acquisition 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.
[§]$p<0.05$; Test for Linear Trend.

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine-Treated F_1 Females (page 1 of 3)

	Atrazine (mg/kg/day, po)		
	0	75	150
No. of Females on Study	15	15	15
Sacrifice Body Weight (g)[a]	184.55 ‡‡‡ ± 4.05 §§§ N=15	169.84 ** ± 2.87 N=15	159.01 *** ± 3.39 N=15
Pituitary Gland Weight (g)[a]	0.0105 ‡‡ ± 0.0004 §§ N=15	0.0099 ± 0.0007 N=14[b]	0.0083 ** ± 0.0003 N=14[b]
Thyroid Gland Weight (g)[a]	0.0193 ± 0.0021 N=14[b]	0.0162 ± 0.0010 N=15	0.0161 ± 0.0012 N=15
Liver Weight (g)[a]	9.7068 ± 0.3705 § N=15	9.0085 ± 0.2131 N=15	8.7233 ± 0.3560 N=15
Paired Adrenal Gland Weight (g)[a]	0.0432 ± 0.0027 N=15	0.0478 ± 0.0022 N=15	0.0414 ± 0.0021 N=15
Paired Kidney Weight (g)[a]	1.8590 ± 0.0490 N=15	1.8054 ± 0.0355 N=15	1.7377 ± 0.0494 N=14[b]
Paired Ovary Weight (g)[a]	0.1015 ‡‡ ± 0.0046 §§ N=15	0.0962 ± 0.0040 N=15	0.0823 ** ± 0.0044 N=15
Uterus with Fluid Weight (g)[a]	0.3694 ± 0.0285 N=15	0.3568 ± 0.0345 N=15	0.3215 ± 0.0251 N=15

(continued)

Table 7-A. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Atrazine-Treated F_1 Females (page 2 of 3)

	Atrazine (mg/kg/day, po)		
	0	75	150
Uterus without Fluid Weight (g)[a]	0.3433 ± 0.0186 N=15	0.3299 ± 0.0223 N=15	0.2965 ± 0.0221 N=15
Adjusted Pituitary Gland Weight (g)[c]	0.0102 ± 0.0006 N=15	0.0099 ± 0.0005 N=14[b]	0.0085 ± 0.0006 N=14[b]
Adjusted Thyroid Gland Weight (g)[c]	0.0200 ± 0.0017 N=14[b]	0.0162 ± 0.0015 N=15	0.0155 ± 0.0016 N=15
Adjusted Liver Weight (g)[c]	8.5691 ŪŪŪ ± 0.1515 ĸĸĸ N=15	9.1185 ?* ± 0.1303 N=15	9.7510 ???* ± 0.1478 N=15
Adjusted Paired Adrenal Gland Weight (g)[c]	0.0426 ± 0.0028 N=15	0.0478 ± 0.0024 N=15	0.0419 ± 0.0027 N=15
Adjusted Paired Kidney Weight (g)[c]	1.7230 Ū ± 0.0318 ĸĸ N=15	1.8187 ± 0.0273 N=15	1.8691 ?* ± 0.0324 N=14[b]
Adjusted Paired Ovary Weight (g)[c]	0.1009 ± 0.0051 ĸ N=15	0.0962 ± 0.0044 N=15	0.0829 ± 0.0050 N=15
Adjusted Uterus with Fluid Weight (g)[c]	0.3644 ± 0.0349 N=15	0.3573 ± 0.0300 N=15	0.3261 ± 0.0340 N=15

(continued)

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

	Atrazine (mg/kg/day, po)		
	0	75	150
Adjusted Uterus without Fluid Weight (g)[c]			
	0.3361 ± 0.0247 N=15	0.3306 ± 0.0213 N=15	0.3030 ± 0.0241 N=15
Thyroxine Hormone (T4) (ug/dL)[a]			
	4.44 ± 0.24 N=15	4.55 ± 0.21 N=15	4.67 ± 0.24 N=15
Thyroid Stimulating Hormone (TSH) (ng/ml)[a]			
	9.62 ± 0.53 N=15	9.90 ± 0.79 N=15	8.52 ± 0.63 N=15

aReported as the mean ± S.E.M.; pnd = postnatal day.
bDecrease in N is due to the organ weight for one animal being a statistical outlier and therefore it was excluded.
cReported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
‡‡p<0.01; ANOVA Test.
‡‡‡p<0.001; ANOVA Test.
§§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 as the covariate.
ƱƱƱp<0.001; Analysis of Covariance with body weight at sacrifice as the covariate.
ʎp<0.05; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
ʎʎp<0.01; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
ʎʎʎp<0.001; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
ϑp<0.05; Dunnett's Test with body weight at sacrifice as the covariate.
ϑϑϑp<0.001; Dunnett's Test with body weight at sacrifice as the covariate.

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Fenarimol-Treated F_1 Females (page 1 of 3)

	Fenarimol (mg/kg/day, po)		
	0	50	250
No. of Females on Study	15	15	15
Sacrifice Body Weight (g)[a]	184.55 ‡‡ ± 4.05 §§§ N=15	185.94 ± 3.43 N=15	166.54 ** ± 3.91 N=15
Pituitary Gland Weight (g)[a]	0.0105 ‡‡ ± 0.0004 §§§ N=15	0.0105 ± 0.0005 N=15	0.0087 ** ± 0.0002 N=15
Thyroid Gland Weight (g)[a]	0.0193 ± 0.0021 N=14[b]	0.0154 ± 0.0011 N=15	0.0151 ± 0.0009 N=15
Liver Weight (g)[a]	9.7068 ‡‡‡ ± 0.3705 §§§ N=15	11.4820 ± 0.3813 N=15	14.1926 *** ± 0.8964 N=15
Paired Adrenal Gland Weight (g)[a]	0.0432 ± 0.0027 N=15	0.0524 ± 0.0030 N=15	0.0441 ± 0.0028 N=15
Paired Kidney Weight (g)[a]	1.8590 ‡ ± 0.0490 § N=15	1.9687 ± 0.0528 N=15	1.7640 ± 0.0435 N=15
Paired Ovary Weight (g)[a]	0.1015 ‡ ± 0.0046 § N=15	0.1106 ± 0.0051 N=15	0.0895 ± 0.0044 N=15
Uterus with Fluid Weight (g)[a]	0.3694 ± 0.0285 N=15	0.3729 ± 0.0255 N=15	0.3118 ± 0.0317 N=15

(continued)

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Fenarimol-Treated F_1 Females (page 2 of 3)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Uterus without Fluid Weight (g)[a]			
	0.3433 ‡ ± 0.0186 §§ N=15	0.3526 ± 0.0201 N=15	0.2782 * ± 0.0187 N=15
Adjusted Pituitary Gland Weight (g)[c]			
	0.0105 ʊ ± 0.0004 ʎʎ N=15	0.0105 ± 0.0004 N=15	0.0088 ʔ* ± 0.0004 N=15
Adjusted Thyroid Gland Weight (g)[c]			
	0.0189 ± 0.0015 N=14[b]	0.0147 ± 0.0014 N=15	0.0161 ± 0.0015 N=15
Adjusted Liver Weight (g)[c]			
	9.1071 ʊʊʊ ± 0.4551 ʎʎʎ N=15	10.7322 ʔ* ± 0.4612 N=15	15.5422 ʔʔʔ* ± 0.4975 N=15
Adjusted Paired Adrenal Gland Weight (g)[c]			
	0.0427 ± 0.0029 N=15	0.0518 ± 0.0030 N=15	0.0452 ± 0.0032 N=15
Adjusted Paired Kidney Weight (g)[c]			
	1.7999 ʊ ± 0.0278 N=15	1.8949 ʔ* ± 0.0282 N=15	1.8968 ± 0.0304 N=15
Adjusted Paired Ovary Weight (g)[c]			
	0.1021 ʊ ± 0.0049 ʎ N=15	0.1113 ± 0.0050 N=15	0.0883 ± 0.0053 N=15
Adjusted Uterus with Fluid Weight (g)[c]			
	0.3712 ± 0.0297 N=15	0.3752 ± 0.0301 N=15	0.3077 ± 0.0325 N=15

(continued)

Table 7-B. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Fenarimol-Treated F_1 Females (page 3 of 3)

	Fenarimol (mg/kg/day, po)		
	0	50	250
Adjusted Uterus without Fluid Weight (g)[c]			
	0.3435 ʊ ± 0.0199 ʎ N=15	0.3529 ± 0.0201 N=15	0.2776 ± 0.0217 N=15
Thyroxine Hormone (T4) (ug/dL)[a]			
	4.44 ‡‡ ± 0.24 §§ N=15	4.72 ± 0.24 N=15	3.73 * ± 0.13 N=15
Thyroid Stimulating Hormone (TSH) (ng/ml)[a]			
#	9.62 ††† ± 0.53 ŸŸŸ N=15	12.53 ÞÞ ± 0.81 N=15	19.65 ÞÞÞ ± 2.29 N=15

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
bDecrease in N is due to the organ weight for one animal being a statistical outlier and therefore it was excluded.
cReported as the adjusted mean ± S.E.M. (sacrifice 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.
ʊp<0.05; Analysis of Covariance with body weight at sacrifice as the covariate.
ʊʊʊp<0.001; Analysis of Covariance with body weight at sacrifice as the covariate.
ʎp<0.05; Linear Trend Analysis of Covariance with body weight at sacrificeas the covariate.
ʎʎp<0.01; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
ʎʎʎp<0.001; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
ʔp<0.05; Dunnett's Test with body weight at sacrifice as the covariate.
ʔʔʔp<0.001; Dunnett's Test with body weight at sacrifice 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.
ÞÞp<0.01; Individual t-test for pairwise comparisons to control in robust regression model.
ÞÞÞp<0.001; Individual t-test for pairwise comparisons to control in robust regression model.

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor-Treated F_1 Females (page 1 of 3)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
No. of Females on Study	15	15	15
Sacrifice Body Weight (g)[a]	184.55 ‡ ± 4.05 § N=15	175.02 ± 3.13 N=14[b]	172.81 * ± 2.85 N=15
Pituitary Gland Weight (g)[a]	0.0105 ± 0.0004 N=15	0.0097 ± 0.0004 N=14	0.0094 ± 0.0005 N=13[c]
Thyroid Gland Weight (g)[a]	0.0193 ± 0.0021 N=14[c]	0.0149 ± 0.0007 N=14	0.0168 ± 0.0008 N=15
Liver Weight (g)[a]	9.7068 ± 0.3705 N=15	8.8628 ± 0.2840 N=14	8.8458 ± 0.2485 N=15
Paired Adrenal Gland Weight (g)[a]	0.0432 ± 0.0027 N=15	0.0439 ± 0.0030 N=14	0.0463 ± 0.0030 N=15
Paired Kidney Weight (g)[a]	1.8590 ± 0.0490 N=15	1.8244 ± 0.0506 N=14	1.7544 ± 0.0511 N=15
Paired Ovary Weight (g)[a]	0.1015 ± 0.0046 § N=15	0.0916 ± 0.0041 N=14	0.0867 ± 0.0049 N=15
Uterus with Fluid Weight (g)[a]	0.3694 ± 0.0285 N=15	0.4092 ± 0.0467 N=14	0.4645 ± 0.0615 N=15

(continued)

Table 7-C. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Methoxychlor-Treated F_1 Females (page 2 of 3)

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Uterus without Fluid Weight (g)[a]	0.3433 ± 0.0186 N=15	0.3504 ± 0.0243 N=14	0.3652 ± 0.0267 N=15
Adjusted Pituitary Gland Weight (g)[d]	0.0103 ± 0.0004 N=15	0.0098 ± 0.0004 N=14	0.0095 ± 0.0005 N=13[c]
Adjusted Thyroid Gland Weight (g)[d]	0.0190 ± 0.0014 N=14[c]	0.0149 ± 0.0014 N=14	0.0170 ± 0.0013 N=15
Adjusted Liver Weight (g)[d]	9.1354 ± 0.1406 N=15	9.0659 ± 0.1392 N=14	9.2277 ± 0.1368 N=15
Adjusted Paired Adrenal Gland Weight (g)[d]	0.0434 ± 0.0030 N=15	0.0438 ± 0.0030 N=14	0.0462 ± 0.0030 N=15
Adjusted Paired Kidney Weight (g)[d]	1.7830 ± 0.0362 N=15	1.8514 ± 0.0358 N=14	1.8052 ± 0.0352 N=15
Adjusted Paired Ovary Weight (g)[d]	0.1029 ± 0.0047 N=15	0.0911 ± 0.0047 N=14	0.0857 ± 0.0046 N=15
Adjusted Uterus with Fluid Weight (g)[d]	0.3865 ± 0.0494 N=15	0.4032 ± 0.0489 N=14	0.4531 ± 0.0480 N=15

(continued)

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

	Methoxychlor (mg/kg/day, po)		
	0	25	50
Adjusted Uterus without Fluid Weight (g)[d]			
	0.3534 ± 0.0241 N=15	0.3468 ± 0.0239 N=14	0.3584 ± 0.0234 N=15
Thyroxine Hormone (T4) (ug/dL)[a]			
	4.44 ± 0.24 N=15	4.57 ± 0.15 N=14	4.69 ± 0.17 N=15
Thyroid Stimulating Hormone (TSH) (ng/ml)[a]			
	9.62 ± 0.53 N=15	8.34 ± 0.47 N=14	9.83 ± 0.98 N=15

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
bAnimal 23 was found dead on the afternoon of postnatal day 38.
cDecrease in N is due to the organ weight for one or more animals being a statistical outlier and therefore it was excluded.
dReported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
‡p<0.05; ANOVA Test.
§p<0.05; Test for Linear Trend.
*p<0.05; Dunnett's Test.
Üp<0.05; Analysis of Covariance with body weight at sacrifice as the covariate.
Λp<0.05; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
Ÿp<0.05; Dunnett's Test with body weight at sacrifice as the covariate.

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Bisphenol A-Treated F_1 Females (page 1 of 3)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
No. of Females on Study	15	15	15
Sacrifice Body Weight (g)[a]	180.17 ‡‡‡ ± 3.11 §§§ N=14[b]	160.62 *** ± 2.76 N=11[c]	155.27 *** ± 3.13 N=14[d]
Pituitary Gland Weight (g)[a]	0.0087 ± 0.0009 N=14	0.0076 ± 0.0006 N=10[e]	0.0075 ± 0.0007 N=14
Thyroid Gland Weight (g)[a]	0.0143 ± 0.0008 N=13[f]	0.0126 ± 0.0005 N=11	0.0134 ± 0.0007 N=14
Liver Weight (g)[a]	9.7498 ‡‡‡ ± 0.3130 §§§ N=14	8.1129 ** ± 0.3039 N=11	7.8492 *** ± 0.2914 N=14
Paired Adrenal Gland Weight (g)[a]	0.0478 ± 0.0029 § N=13[e]	0.0414 ± 0.0019 N=11	0.0412 ± 0.0016 N=14
Paired Kidney Weight (g)[a]	1.8109 ‡‡ ± 0.0530 §§ N=14	1.6321 * ± 0.0432 N=11	1.5900 ** ± 0.0489 N=14
Paired Ovary Weight (g)[a]	0.1009 ‡‡‡ ± 0.0048 §§§ N=14	0.0734 *** ± 0.0050 N=11	0.0663 *** ± 0.0048 N=14
Uterus with Fluid Weight (g)[a]	0.3276 ± 0.0261 § N=14	0.2695 ± 0.0212 N=11	0.2436 ± 0.0293 N=14

(continued)

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Bisphenol A-Treated F_1 Females (page 2 of 3)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Uterus without Fluid Weight (g)[a]	0.3057 ‡ ± 0.0255 §§ N=14	0.2532 ± 0.0214 N=11	0.2080 ** ± 0.0203 N=14
Adjusted Pituitary Gland Weight (g)[g]	0.0071 ± 0.0008 N=14	0.0082 ± 0.0008 N=10[e]	0.0087 ± 0.0007 N=14
Adjusted Thyroid Gland Weight (g)[g]	0.0136 ± 0.0008 N=13[f]	0.0128 ± 0.0007 N=11	0.0139 ± 0.0007 N=14
Adjusted Liver Weight (g)[g]	8.4459 ± 0.1628 N=14	8.5728 ± 0.1468 N=11	8.7918 ± 0.1464 N=14
Adjusted Paired Adrenal Gland Weight (g)[g]	0.0419 ± 0.0025 N=13[e]	0.0433 ± 0.0021 N=11	0.0452 ± 0.0021 N=14
Adjusted Paired Kidney Weight (g)[g]	1.6342 ± 0.0411 N=14	1.6945 ± 0.0370 N=11	1.7177 ± 0.0369 N=14
Adjusted Paired Ovary Weight (g)[g]	0.0917 ± 0.0057 ⁄ N=14	0.0766 ± 0.0051 N=11	0.0729 ± 0.0051 N=14
Adjusted Uterus with Fluid Weight (g)[g]	0.3012 ± 0.0327 N=14	0.2788 ± 0.0295 N=11	0.2627 ± 0.0294 N=14

(continued)

Table 7-D. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Bisphenol A-Treated F_1 Females (page 3 of 3)

	Bisphenol A (mg/kg/day, po)		
	0	400	600
Adjusted Uterus without Fluid Weight (g)[g]			
	0.2768 ± 0.0278 N=14	0.2634 ± 0.0250 N=11	0.2290 ± 0.0250 N=14
Thyroxine Hormone (T4) (ug/dL)[a]			
	4.81 ± 0.27 N=14	4.88 ± 0.24 N=11	5.23 ± 0.24 N=14
Thyroid Stimulating Hormone (TSH) (ng/mL)[a]			
	7.88 ± 0.41 N=14	6.97 ± 0.30 N=11	7.51 ± 0.42 N=14

aReported as the mean ± S.E.M.; pnd = postnatal day.
bAnimal 1 was found dead on the morning of postnatal day 40.
cAnimal 16 was found dead on the morning of postnatal day 28; animal 27 was found dead after dosing on postnatal day 30; animal 59 was found dead on the morning of postnatal day 27; and animal 87 was euthanized moribund after dosing on postnatal day 34.
dAnimal 46 was found dead after dosing on postnatal day 29.
eDecrease in N is due to the organ weight for one animal being a statistical outlier and therefore it was excluded.
fDecrease in N is due to the thyroid gland not being saved for one animal and therefore a fixed weight could not be obtained.
gReported as the adjusted mean ± S.E.M. (sacrifice 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.
⁄p<0.05; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole-Treated F_1 Females (page 1 of 3)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
No. of Females on Study	15	15	15
Sacrifice Body Weight (g)[a]			
	180.17 ‡ ± 3.11 §§ N=14[b]	178.34 ± 3.27 N=15	166.37 * ± 3.52 N=15
Pituitary Gland Weight (g)[a]			
#	0.0087 ± 0.0009 N=14	0.0088 ± 0.0005 N=14[c]	0.0080 ± 0.0004 N=15
Thyroid Gland Weight (g)[a]			
	0.0143 ± 0.0008 N=13[d]	0.0147 ± 0.0005 N=15	0.0144 ± 0.0007 N=15
Liver Weight (g)[a]			
	9.7498 ± 0.3130 N=14	10.7657 ± 0.2997 N=15	10.5637 ± 0.3982 N=15
Paired Adrenal Gland Weight (g)[a]			
	0.0478 ‡‡‡ ± 0.0029 §§§ N=13[c]	0.0799 *** ± 0.0039 N=15	0.0785 *** ± 0.0037 N=14[e]
Paired Kidney Weight (g)[a]			
	1.8109 ± 0.0530 § N=14	1.9571 ± 0.0519 N=15	1.9827 ± 0.0581 N=15
Paired Ovary Weight (g)[a]			
	0.1009 ‡ ± 0.0048 § N=14	0.0968 ± 0.0051 N=14[f]	0.0843 * ± 0.0037 N=15
Uterus with Fluid Weight (g)[a]			
	0.3276 ‡ ± 0.0261 §§ N=14	0.2981 ± 0.0239 N=15	0.2390 * ± 0.0158 N=15

(continued)

Table 7-E. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Ketoconazole-Treated F_1 Females (page 2 of 3)

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Uterus without Fluid Weight (g)[a]			
	0.3057 ‡ ± 0.0255 §§ N=14	0.2730 ± 0.0172 N=15	0.2217 ** ± 0.0152 N=15
Adjusted Pituitary Gland Weight (g)[g]			
	0.0084 ± 0.0008 N=14	0.0085 ± 0.0005 N=14[c]	0.0085 ± 0.0005 N=15
Adjusted Thyroid Gland Weight (g)[g]			
	0.0140 ± 0.0007 N=13[d]	0.0145 ± 0.0006 N=15	0.0149 ± 0.0007 N=15
Adjusted Liver Weight (g)[g]			
	9.2651 ŬŬŬ ± 0.1696 ʎʎʎ N=14	10.4472 ??? ± 0.1613 N=15	11.3346 ??? ± 0.1716 N=15
Adjusted Paired Adrenal Gland Weight (g)[g]			
	0.0448 ŬŬŬ ± 0.0035 ʎʎʎ N=13[c]	0.0781 ??? ± 0.0032 N=15	0.0833 ??? ± 0.0036 N=14[e]
Adjusted Paired Kidney Weight (g)[g]			
	1.7423 ŬŬŬ ± 0.0361 ʎʎʎ N=14	1.9120 ?? ± 0.0343 N=15	2.0919 ??? ± 0.0365 N=15
Adjusted Paired Ovary Weight (g)[g]			
	0.0983 ± 0.0044 N=14	0.0948 ± 0.0044 N=14[f]	0.0886 ± 0.0045 N=15
Adjusted Uterus with Fluid Weight (g)[g]			
	0.3182 ± 0.0228 N=14	0.2920 ± 0.0217 N=15	0.2540 ± 0.0231 N=15

(continued)

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

	Ketoconazole (mg/kg/day, po)		
	0	50	100
Adjusted Uterus without Fluid Weight (g)[g]			
	0.2969 ± 0.0200 ʎ N=14	0.2672 ± 0.0190 N=15	0.2357 ± 0.0202 N=15
Thyroxine Hormone (T4) (ug/dL)[a]			
	4.81 ± 0.27 N=14	4.97 ± 0.16 N=15	4.79 ± 0.19 N=15
Thyroid Stimulating Hormone (TSH) (ng/ml)[a]			
	7.88 ± 0.41 N=14	8.91 ± 0.82 N=15	8.24 ± 0.47 N=14[h]

[a]Reported as the mean ± S.E.M.; pnd = postnatal day.
[b]Animal 1 was found dead on the morning of postnatal day 40.
[c]Decrease in N is due to the organ weight for one animal being a statistical outlier and therefore it was excluded.
[d]Decrease in N is due to the thyroid gland not being saved for one animal and therefore a fixed weight could not be obtained.
[e]Decrease in N is due to the study sponsor requesting that the paired adrenal gland weight for animal 53 be excluded.
[f]Decrease in N is due to one animal having only a right ovary therefore a paired ovary weight could not be obtained.
[g]Reported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
[h]Decrease in N is due to there not being sufficient sample to perform the assay for one animal, although a sample from this animal was assayed in a validation test and had a value of 7.59 ng/ml.
‡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.
ʊʊʊp<0.001; Analysis of Covariance with body weight at sacrifice as the covariate.
ʎp<0.05; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
ʎʎʎp<0.001; Linear Trend Analysis of Covariance with body weight at sacrifice as the covariate.
ϑϑϑp<0.001; Dunnett's Test with body weight at sacrifice as the covariate.

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil-Treated F_1 Females (page 1 of 3)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
No. of Females on Study	15	15	15
Sacrifice Body Weight (g)[a]			
	180.17 ‡‡‡ ± 3.11 §§§ N=14[b]	175.25 ± 2.50 N=15	130.32 *** ± 2.60 N=15
Pituitary Gland Weight (g)[a]			
	0.0087 ± 0.0009 N=14	0.0085 ± 0.0006 N=15	0.0075 ± 0.0005 N=15
Thyroid Gland Weight (g)[a]			
#	0.0143 ††† ± 0.0008 ŸŸŸ N=13[c]	0.0385 ÞÞÞ ± 0.0016 N=15	0.0620 ÞÞÞ ± 0.0048 N=15
Liver Weight (g)[a]			
	9.7498 ‡‡‡ ± 0.3130 §§§ N=14	9.0381 ± 0.2596 N=15	5.8020 *** ± 0.2095 N=15
Paired Adrenal Gland Weight (g)[a]			
	0.0478 ‡‡‡ ± 0.0029 §§§ N=13[d]	0.0420 ± 0.0020 N=15	0.0277 *** ± 0.0010 N=13[d]
Paired Kidney Weight (g)[a]			
	1.8109 ‡‡‡ ± 0.0530 §§§ N=14	1.7156 ± 0.0420 N=15	1.2506 *** ± 0.0942 N=15
Paired Ovary Weight (g)[a]			
	0.1009 ‡‡‡ ± 0.0048 §§§ N=14	0.0893 ± 0.0037 N=15	0.0756 *** ± 0.0037 N=15
Uterus with Fluid Weight (g)[a]			
	0.3276 ± 0.0261 N=14	0.3449 ± 0.0270 N=15	0.3408 ± 0.0363 N=15

(continued)

Table 7-F. Summary and Statistical Analysis of the Organ Weights and Hormone Data for the Propylthiouracil-Treated F_1 Females (page 2 of 3)

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Uterus without Fluid Weight (g)[a]	0.3057 ± 0.0255 N=14	0.3192 ± 0.0229 N=15	0.3015 ± 0.0208 N=15
Adjusted Pituitary Gland Weight (g)[e]	0.0071 ± 0.0009 N=14	0.0073 ± 0.0008 N=15	0.0102 ± 0.0013 N=15
Adjusted Thyroid Gland Weight (g)[e]			
#	0.0077 ♦♦♦ ± 0.0041 △△△ N=13[c]	0.0334 ◁◁◁ ± 0.0035 N=15	0.0728 ◁◁◁ ± 0.0096 N=15
Adjusted Liver Weight (g)[e]	8.2414 ± 0.2103 N=14	7.9265 ± 0.1797 N=15	8.3215 ± 0.2898 N=15
Adjusted Paired Adrenal Gland Weight (g)[e]	0.0449 ± 0.0032 N=13[d]	0.0399 ± 0.0026 N=15	0.0330 ± 0.0049 N=13[d]
Adjusted Paired Kidney Weight (g)[e]	1.6368 ± 0.0937 N=14	1.5873 ± 0.0800 N=15	1.5414 ± 0.1291 N=15
Adjusted Paired Ovary Weight (g)[e]	0.0907 ± 0.0056 N=14	0.0817 ± 0.0048 N=15	0.0926 ± 0.0078 N=15
Adjusted Uterus with Fluid Weight (g)[e]	0.3288 ± 0.0454 N=14	0.3458 ± 0.0388 N=15	0.3389 ± 0.0626 N=15

(continued)

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

	Propylthiouracil (mg/kg/day, po)		
	0	2	25
Adjusted Uterus without Fluid Weight (g)[e]			
	0.2860 ± 0.0342 N=14	0.3047 ± 0.0292 N=15	0.3343 ± 0.0472 N=15
Thyroxine Hormone (T4) (ug/dL)[a]			
#	4.81 ††† ŸŸŸ ± 0.27 N=14	1.97 ÞÞÞ ± 0.27 N=14[f]	0.66 ÞÞÞ ± 0.02 N=2[f]
Thyroid Stimulating Hormone (TSH) (ng/ml)[a]			
#	7.88 ††† ŸŸŸ ± 0.41 N=14	42.36 ÞÞÞ ± 6.14 N=15	99.41 ÞÞÞ ± 5.67 N=15

aReported as the mean ± S.E.M.; pnd = postnatal day.
bAnimal 1 was found dead on the morning of postnatal day 40.
cDecrease in N is due to the thyroid gland not being saved for one animal and therefore a fixed weight could not be obtained.
dDecrease in N is due to the organ weight for one or more animals being a statistical outlier and therefore it was excluded.
eReported as the adjusted mean ± S.E.M. (sacrifice weight as covariate).
fDecrease in N is due to the hormone concentration for one or more animals being below the minimum detectable limit.
#Levene's test for homogeneity of variances was significant ($p<0.05$) or there was an N of less than 3 in one or more groups and the Levene's test dropped those groups, 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<0.001; 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.
♦♦♦p<0.001; Wald Chi-square Test for overall treatment effect in robust regression model with body weight at sacrifice as the covariate.
△△△p<0.001; Linear trend test in robust regression model with body weight at sacrifice as the covariate.
◁◁◁p<0.001; Individual t-test for pairwise comparisons in robust regression model with body weight at sacrifice as the covariate.

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

A. Scheduled Necropsy

	Atrazine (mg/kg/day, po)		
Finding	0	75	150
Kidney: hydronephrosis, right	1		1
Uterus: 5 mm diameter cyst, right horn			1
clear fluid filled		1	
fluid filled	1		

Table 8-B. Summary of Necropsy Findings for the Fenarimol-Treated F_1 Females (page 1 of 1)

A. Scheduled Necropsy

	Fenarimol (mg/kg/day, po)		
Finding	0	50	250
Kidney: hydronephrosis, bilateral		1	1
hydronephrosis, right	1		
Uterus: ½ length of other horn, right horn			1
two 3 mm diameter cysts, right horn		1	
clear fluid filled		1	
fluid filled	1	1	3
fluid filled, left horn			1

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

A. Scheduled Necropsy

	Methoxychlor (mg/kg/day, po)		
Finding	0	25	50
Kidney: hydronephrosis, bilateral			1
hydronephrosis, left		1	
hydronephrosis, right	1		
Uterus: clear fluid filled		1	2
fluid filled	1	1	4

B. Unscheduled Necropsy

	Methoxychlor (mg/kg/day, po)		
Finding	0	25	50
Lungs: congested, oil present; probable aspiration of dosing solution/suspension		1	

Table 8-D. Summary of Necropsy Findings for the Bisphenol A-Treated F_1 Females (page 1 of 1)

A. Scheduled Necropsy

	Bisphenol A (mg/kg/day, po)		
Finding	0	400	600
Kidney: hydronephrosis, bilateral			1
hydronephrosis, left			1
hydronephrosis, right	3		1

B. Unscheduled Necropsy

	Bisphenol A (mg/kg/day, po)		
Finding	0	400	600
Kidney: 7 mm x 5 mm dark spot, left	1		
Lungs: congested, all lobes dark red		1	
dosing solution/suspension present	1		

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

A. Scheduled Necropsy

	Ketoconazole (mg/kg/day, po)		
Finding	0	50	100
Adrenal Gland: enlarged and pale, bilateral		1	
enlarged, bilateral		3	4
pale gray, bilateral			1
pale, bilateral		4	
Kidney: hydronephrosis, bilateral		2	
hydronephrosis, right	3		
Ovary: missing. left		1	

B. Unscheduled Necropsy

	Ketoconazole (mg/kg/day, po)		
Finding	0	50	100
Kidney: 7 mm x 5 mm dark spot, left	1		
Lungs: dosing solution/suspension present	1		

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

A. Scheduled Necropsy

	Propylthiouracil (mg/kg/day, po)		
Finding	0	2	25
Kidney: hydronephrosis, bilateral		1	1
hydronephrosis, right	3	2	
misshapened and pale and polycystic, right			1
Thyroid Gland: enlarged and reddened, bilateral			1
enlarged, bilateral			1
Uterus: fluid filled			1

B. Unscheduled Necropsy

	Propylthiouracil (mg/kg/day, po)		
Finding	0	2	25
Kidney: 7 mm x 5 mm dark spot, left	1		
Lungs: dosing solution/suspension present	1		

FINAL REPORT
APPENDICES II - V

Assessment of Pubertal Development and Thyroid Function in Juvenile Female CD® (Sprague-Dawley) Rats After Exposure to Selected Chemicals Administered by Gavage on Postnatal Days 22 to 42/43

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Study Initiation Date:

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(Component 2)

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APPENDIX I

Individual Animal Data Tables

Appendix II

Histopathology Report

Appendix III

Analytical Chemistry Reports

Appendix IV

Feed Analysis Reports

Appendix V

Protocol and Two Amendments