14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

FINAL REPORT

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Study Initiation Date: **May 5, 2004**
Study Completion Date: **December 14, 2004**

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

ABSTRACT

Male and female Fischer 344 rats (15/sex/group) were dosed by intravenous injection once daily for 14 consecutive days with a 14-day recovery period to evaluate the potential toxicity of CuATSM/H_2ATSM (NSC-D729307). The test article was administered in a vehicle consisting of dimethyl sulfoxide (0.3% v/v), ethanol (7.0% v/v) and saline (0.9% sodium chloride for injection USP; 92.7% v/v) at target doses of 0.075 and 0.150 mg/kg/day (Groups 2 and 3, respectively). A vehicle control group (Group 1) was administered vehicle only once daily for 14 consecutive days.

No animals died during the study. No treatment-related clinical signs were observed during the study. No treatment-related effects on mean body weights and mean body weight gains were observed during the study and no treatment-related or toxicologically significant changes were observed in any of the functional observational battery parameters evaluated at pretest (baseline) and on Study Days 14 and 28. There were no toxicologically significant changes for any clinical pathology (clinical chemistry and hematology) parameter evaluated on Study Days 8, 15 and 29. Evaluation of bone marrow erythrocytes for micronuclei showed no treatment-related responses on Study Day 15. At terminal and recovery necropsies (Study Days 15 and 29, respectively), no treatment-related or toxicologically significant effects were observed in the mean absolute and relative (*i.e.*, organ-to-body weight ratios) organ weights in either sex. All of the gross and histopathologic findings were considered incidental and unrelated to treatment.

In summary, during a 14-day treatment period of intravenous administration of CuATSM/H_2ATSM, there were no treatment-related and/or toxicologically significant effects for any of the parameters evaluated. Thus, based on these data, the no-observed-adverse-effect level (NOAEL) for this study was the 0.150 mg/kg/day of CuATSM/H_2ATSM.

COMPREHENSIVE SUMMARY

Title:	14-Day Toxicity Study of CuATSM / H_2ATSM (NSC-D729307) in Rats
Species:	Rat
Strain:	Fischer 344 [CDF(F-344)/CrlBR]
Sex:	Male and female
Age:	Approximately 9 weeks (at arrival); approximately 10 weeks [at dosing initiation (*i.e.*, Study Day 1)]
Body Weight:	158 g to 167 g (males) and from 119 g to 132 g (females) (based on representative sample of eight animals per sex, one day after receipt)
Dose Groups:	Group 1 (Vehicle Control): 0 mg CuATSM/H_2ATSM/kg/day Group 2 (Low Dose): 0.075 mg CuATSM/H_2ATSM/kg/day Group 3 (High Dose): 0.150 mg CuATSM/H_2ATSM/kg/day Group 4 (Positive Control): 30 mg cyclophosphamide/kg; used for bone marrow evaluation (untreated with test article)
Dose Schedule:	Once daily for 14 consecutive days
Number of Animals:	100 [65 Main Study (10/sex/group in Groups 1-3; 5 males in Group 4) + 35 Recovery (5/sex/group in Groups 1-3; 5 males in Group 4)]
Dose Route:	Intravenous injection
Test Article:	CuATSM / H_2ATSM (NSC-D729307)
Vehicle:	mixture of dimethyl sulfoxide (0.3% v/v), ethanol (7% v/v) and saline (0.9% sodium chloride for injection USP; 92.7% v/v)

RESULTS:

Mortality:	No animals died during the study.
Clinical Observations:	No treatment-related clinical signs were observed.
Body Weights and Body Weight Gains:	No treatment-related effects on mean body weights or mean body weight gains were observed during the study.
Functional Observational Battery (FOB):	No treatment-related, toxicologically significant or otherwise noteworthy changes were observed for any of the FOB parameters evaluated at pre-study (baseline) or on Study Days 14 and 28.

Clinical Chemistry: The following statistically significant changes were observed (as compared to the vehicle control group): decreased blood urea nitrogen (non-fasted low- and high-dose females on Study Day 8); increased blood urea nitrogen (non-fasted low-dose females on Study Day 15); decreased albumin (fasted low-dose females on Study Day 15); increased cholesterol levels (non-fasted low- and high-dose males on Study Day 15); and increased triglyceride (fasted high-dose males on Study Day 15). No consistent pattern of treatment-related, toxicologically significant or dose-related effects was apparent and these changes were not considered drug-related. No other clinical chemistry effects were observed.

Hematology: The following statistically significant changes were observed (as compared to the vehicle control group): increased red blood cell counts (non-fasted low- and high-dose males on Study Day 8 and fasted low-dose males on Study Day 15); increased absolute large unstained cell count (non-fasted high-dose males on Study Day 8); increased relative large unstained cell counts (non-fasted low- and high-dose males on Study Day 8); decreased relative reticulocyte counts (non-fasted low- and high-dose males on Study Day 8); increased absolute and relative monocyte counts (fasted low- and high-dose males on Study Day 15); decreased mean corpuscular volume (fasted low-dose males on Study Day 15); increased mean corpuscular hemoglobin concentration (fasted low-dose males on Study Day 15); and decreased relative eosinophil count (fasted low-dose females on Study Day 29). No consistent pattern of treatment-related, toxicologically significant or dose-related effects was apparent and these changes were not considered drug-related. No other hematology effects were observed.

Bone Marrow Mutagenicity: There were no effects on mean micronucleated polychromatic erythrocyte (MPCE) count [*i.e.*, log(MPCE+1)] or mean percent of polychromatic erythrocytes (%PCE) on either Study Day 15 or 29.

Organ Weights: The following statistically significant changes were observed (as compared to the vehicle control group): increased mean absolute and relative (*i.e.*, organ-to-body weight ratio) adrenals weights (low-dose females on Study Day 15); decreased mean relative heart weight (low-dose males on Study Day 29); and decreased mean absolute and relative heart weights (high-dose females on Study Day 29). All the observed organ weight effects were not considered toxicologically significant. No other organ weight effects were observed.

Gross Necropsy: All of the gross lesions observed at necropsy were interpreted as incidental findings typically present in rat toxicology studies.

Histopathology: No remarkable microscopic changes were observed which were considered treatment-related.

CONCLUSION: There were no treatment-related and/or toxicologically significant effects for any parameter evaluated. Based on these findings, the no-observed-adverse-effect level (NOAEL) for this study is 0.150 mg/kg body weight/day of CuATSM/H_2ATSM.

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Study Initiation Date: May 5, 2004
Experimental Initiation Date: May 6, 2004
In-Life Study Completion Date: June 3, 2004

FOREWORD

This report describes a 14-day intravenous toxicity study conducted by IIT Research Institute (IITRI) for the National Cancer Institute (NCI). The NCI Project Officer for the study was Elizabeth R. Glaze, Ph.D.

Thomas L. Horn, Ph.D., served as Study Director and was responsible for the overall conduct of the study. David L. McCormick, Ph.D., D.A.B.T., Vice President and Director, Life Sciences Group, served as Principal Investigator. J. Brooks Harder, D.V.M., IITRI staff veterinarian, was responsible for animal care. Mary Ann Cahill, B.S., M.T. (A.S.C.P.), was responsible for the clinical pathology evaluations. Patrick T. Curry, Ph.D., Senior Biologist, was responsible for the evaluation of the bone marrow smears for the presence of micronuclei. Carol Detrisac, D.V.M., Ph.D., D.A.C.V.P., of Pathology Associates (A Division of Charles River Laboratories, Inc., Chicago, IL), Study Pathologist, supervised the terminal necropsies and performed the microscopic tissue examinations. Glenn B. Miller, M.S., C.Q.M., Manager, Quality Assurance, was responsible for quality assurance.

Thomas L. Horn, Ph.D. 12/14/04
Study Director Date
Life Sciences Group

David L. McCormick, Ph.D., D.A.B.T. 12/14/04
Principal Investigator Date
Vice President and Director
Life Sciences Group

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

GLP COMPLIANCE STATEMENT

This study was conducted in accordance with the U.S. Food and Drug Administration (FDA) Good Laboratory Practice Regulations (Title 21, Part 58 of the *Code of Federal Regulations*) with the following exceptions: characterization of the test article is the responsibility of the Sponsor, and the analysis of the test article and vehicle control dosing formulations were not performed according to Good Laboratory Practice Regulations. The study raw data have been reviewed and the information contained in this report is an accurate representation of the study data and represents an appropriate and accurate conclusion within the context of the study design and evaluation criteria.

Thomas L. Horn, Ph.D. — Date
Study Director
Life Sciences Group

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14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

I. INTRODUCTION

The objective of this study was to determine the target organ toxicity of CuATSM / H_2ATSM (NSC-D729307) and its reversibility when administered intravenously to rats once a day for 14 days.

II. MATERIALS AND METHODS

A list of abbreviations used in this report and their definitions is given in Table 1. Copies of the study protocol and protocol amendment are included as Appendix A.

A. Test and Control Articles: The test article, identified as NSC-D729307 [also identified as copper-diacetyl-bis (N^4-methylthiosemicarbazone)/diacetyl-bis (N^4-methylthiosemicarbazone) or CuATSM/H_2ATSM], a blue-gray powder, and not bearing a lot number, was received October 9, 2003. The test article was protected from light and stored in its original container at room temperature. The identity, strength, quality, stability and purity, as well as documentation of methods of synthesis, fabrication or derivation, were the responsibility of the Sponsor. One control article was dimethyl sulfoxide (DMSO), purchased from Sigma-Aldrich, St. Louis, MO (lot number 033K0640). A second control article was ethanol (EtOH; 100%), purchased from Pharmco Products, Inc., Brookfield, CT (lot number PS5520). A third control article was 0.9% sodium chloride for injection (saline; USP; Baxter Healthcare Corp., Deerfield, IL; lot number C604942). The positive control article, cyclophosphamide, an off-white powder, was purchased from Sigma-Aldrich, Milwaukee, WI (lot number 11320MS). The control articles were stored in their original containers at room temperature; the positive control was stored refrigerated. The control articles were considered characterized by their accompanying documentation. Copies of the test article Data Sheets and Certificates of Analysis for the control articles are included in Appendix B.

B. Test Article and Vehicle Dose Formulation Preparation: The vehicle control consisted of a mixture of the control articles DMSO (0.3% v/v), EtOH (7% v/v) and saline (92.7% v/v). Test article was dissolved in DMSO to produce a stock solution (approximately 10 mg/ml). The stock solution was aliquotted and further diluted with DMSO as necessary, and then 100% ethanol and saline were added to produce the target dosing

concentrations. The test article stock solution, each test article dosing formulation and the vehicle control were prepared fresh daily. When not in use, the test article dosing formulations were stored in the dark at room temperature (approximately 20-25°C). Cyclophosphamide was dissolved in saline. When not in use, the cyclophosphamide dosing formulation was stored refrigerated (approximately 2-8°C). The target concentrations, based on solubility of the test article in vehicle, were determined such that all animals were to be dosed at constant dosing volume of 5 ml/kg body weight/dose. Target concentrations of the dose formulations were 0.015 mg/ml (low dose) and 0.030 mg/ml (high dose) of CuATSM/H_2ATSM in the vehicle [DMSO (0.3%)/EtOH (7%)/saline (92.7%)]. Samples of the test article and vehicle control formulations were obtained on Study Days 1, 8 and 14 and were stored frozen until shipped to a Sponsor-designated laboratory (Dr. Ruiwen Zhang, Department of Pharmacology and Toxicology, University of Alabama at Birmingham, Birmingham, AL) for analysis for concentration (Study Days 1, 8 and 14), homogeneity (Study Day 1) and stability (Study Days 1, 8 and 14) on June 1, 2004. The following table illustrates the preparation of stock solution, vehicle control and dosing formulations during Week 1 of the study. (Procedures were the same for both weeks, although specific amounts, *i.e.,* total volumes prepared, varied.)

Group	Targeted Dose Conc.	Formulation of Test Article
All	Stock solution	10 mg CuATSM/H_2ATSM in 1.0 ml DMSO (prepared daily)
1	0.0 mg/ml (Vehicle Control)	mix 120 µl DMSO with 2.8 ml EtOH, *q.s* to 40 ml with saline – filter sterilize (prepared daily)
2	0.015 mg/ml (0.075 mg/kg/day)	mix 60 µl stock solution with 60 µl DMSO with 2.8 ml EtOH, *q.s.* to 40 ml with saline – filter sterilize (prepared daily)
3	0.030 mg/ml (0.150 mg/kg/day)	mix 120 µl stock solution with 2.8 ml EtOH, *q.s* .to 40 ml with saline – filter sterilize (prepared daily)

The positive control was prepared and used for dosing on Study Day 14. The positive control was prepared on Study Day 27 and stored refrigerated until used for dosing on Study Day 28. Cyclophosphamide was at a concentration of 15 mg/ml. The saline used to prepare the positive control dosing formulation was a different lot from that used for preparing the stock, test article and vehicle control dosing formulations. Analyses for positive control dose formulation concentration, homogeneity and stability were not performed.

C. Animals, Housing and Diet: Sixty-one (61) male and 51 female Fischer rats [CDF(F-344)/CrlBR rats], approximately 9 weeks of age, were received on April 27, 2004, from Charles River Laboratories, Raleigh, NC, for use in this study. One day after arrival, the body weights of a representative sample of eight animals per sex ranged from 158 g to 167 g (males) and from 119 g to 132 g (females). Rats were housed in stainless steel cages equipped with automatic watering systems. Absorbent cageboards were placed underneath the cages to contain liquid and solid wastes. Rats were housed two per cage (except one single-housed female and three triple-housed males) for nine days. Study animals were individually housed at randomization (May 4, 2004) and for the duration of the study. Animals were housed in accordance with the *Guide for Care and Use of Laboratory Animals* (National Research Council, 1996). Each rat was identified by means of a metal ear tag bearing an animal number unique within the study. Each rat cage was identified with a card bearing the project number, group number, animal number and sex.

Animal room temperature and relative humidity values were recorded once daily during the quarantine period and twice daily during the treatment and recovery periods. Temperature ranged from 19.8 to 23.7°C and relative humidity ranged from 30 to 68% during the study. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness.

Certified Rodent Laboratory Chow #5002 (PMI Nutrition International, Brentwood, MO) was provided *ad libitum* to all rats throughout the study, except for overnight fasts prior to scheduled necropsy. City of Chicago municipal water was available *ad libitum* via an automatic watering system. Based on analysis reports for the diet provided by the vendor and external water analysis reports, no contaminants were known to be present in the food or water at levels expected to interfere with the outcome of the study.

D. Quarantine: Animals were held in quarantine for nine days prior to dosing, during which time they were observed daily for survival and general health. Animals were examined carefully to ensure their health and suitability as test subjects prior to randomization into experimental groups. Animals were randomized using an in-house developed, computer-based body weight stratification procedure on May 4, 2004.

E. Experimental Design: After randomization, 100 rats (15/sex/group in Groups 1-3; 10 males in positive control Group 4) were assigned to two test article dose groups, a vehicle control group and a positive control group as follows:

Group	Targeted Daily Dose CuATSM/H_2ATSM		Number of Rats at Treatment Start (M + F)	Number of Rats Sacrificed	
	(mg/kg/day)	(mg/m^2/day)		Day 15 (M + F)	Day 29 (M + F)
1	0.000	0.00	15 + 15	10 + 10	5 + 5
2	0.075	0.45	15 + 15	10 + 10	5 + 5
3	0.150	0.90	15 + 15	10 + 10	5 + 5
4	Cyclophosphamide (30mg/kg)		10 + 0	5 + 0	5 + 0

Animals (except Group 4) were dosed daily for 14 consecutive days starting on May 6, 2004. Sixty rats (10/sex/group in Groups 1-3) were sacrificed on Study Day 15 (May 20, 2004). The remaining rats in Groups 1-3 were observed for 14 days thereafter and were sacrificed on Study Day 29 (June 3, 2004). Group 4 rats consisted of 10 male rats only and were used as a positive control for the bone marrow micronucleus assays (see Section II.F.7 below); five rats each were administered a single intravenous injection of cyclophosphamide on Study Day 14 or 28 and sacrificed 18-24 hours later. All rats were approximately 10 weeks of age at dosing initiation.

F. Methods

1. Test Article and Vehicle Administration: Starting on Study Day 1 and for 14 consecutive days, the CuATSM/H_2ATSM dose formulations were administered to each rat in the test article treatment groups by slow bolus intravenous injection. Rats in the vehicle control group were dosed similarly with an equivalent volume of vehicle (DMSO/EtOH/saline) only. The amount of drug administered to each rat was based on its most recently determined body weight and all rats in Groups 1-3 were dosed with a uniform volume of 5 ml/kg body weight. Rats in Group 4 (positive control) were also dosed with cyclophosphamide (30 mg/kg) once at a dosing volume of 2 ml/kg body weight on Study Day 14 or 28.

2. Mortality/Moribundity Observations: Rats were observed for moribundity and mortality once daily during quarantine and twice daily throughout the treatment and

recovery periods. Mortality/moribundity checks were separated by a minimum of four hours.

3. Clinical Observations and Physical Examinations: A detailed hand-held physical and clinical observation was performed on all animals during the quarantine period prior to randomization to ensure suitability for use as a test animal and on all surviving study animals in Groups 1-3 weekly throughout the treatment and recovery periods. Cageside clinical observations were recorded daily for animals in Groups 1-3. Weekly observations during the treatment and recovery periods were recorded by electronic data capture (LABCAT, IPA Inc., Princeton, NJ, version 4.65).

4. Body Weights: Body weights were measured one day after the rats were received (random sample of eight rats/sex), and on all rats once during quarantine (randomization). All study animals in Groups 1-3 were weighed on Study Days 1, 5, 8, 12, 15 and twice weekly during the recovery period. In addition, rats scheduled for necropsy on Study Days 15 and 29 were fasted overnight and final fasted body weights were determined. Group 4 rats that were sacrificed on Study Day 15 were weighed on Study Day 14, and Group 4 rats that were sacrificed on Study Day 29 were weighed on Study Day 28. In general, all study rats were weighed at approximately the same time each day between 7 and 11 am. Body weight determinations were also included as part of the Functional Observational Battery (FOB) evaluations. Following randomization, body weight data were recorded, and body weight gains were calculated, using electronic data capture (LABCAT, IPA Inc., Princeton, NJ, version 4.65) with the exception of the FOB body weights collected on Study Day -2 and the Group 4 body weights collected on Study Day 14 or 28.

5. Functional Observational Battery (FOB): The last ten (numerically) surviving rats/sex/group in Groups 1-3 were evaluated with an FOB on Study Day -2 to -1 (pretest), Study Day 14 and Study Day 28 (recovery rats only). During the treatment period, these evaluations were performed approximately two to four hours after dosing, with the exception of the FOB body weights. FOB body weights were collected on the day the FOB was performed (except at pretest); however, body weight data were measured prior to the collection of the first FOB parameter (*i.e.*, home cage observation). The following parameters were monitored: home cage observation, handheld observation, audition (click), body temperature, open field

(mobility/gait), tail pinch, pupil response, eye blink response, vision, hindlimb extension, catalepsy, grip strength (forelimb and hindlimb), righting reflex, foot splay and body weights.

6. Clinical Pathology: Blood samples for analysis of hematology and clinical chemistry were collected from the last ten (numerically) study animals per sex per group in Groups 1-3 on Study Days 8 (unfasted) and 15 (fasted for scheduled necropsy rats and unfasted for recovery rats). Blood samples for hematology and clinical chemistry were collected from all surviving recovery rats on Study Day 29 (fasted). All blood samples were collected from rats anesthetized with CO_2/air (70%/30%) via retro-orbital sinus puncture.

   Hematological parameters evaluated using the ADVIA 120 Hematology System (Bayer Corp., Tarrytown, NY) consisted of erythrocyte count, hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), platelet count, total leukocyte count, absolute and relative differential leukocyte counts and absolute and relative reticulocyte counts.

   The following clinical chemistry parameters were evaluated using a Beckman Coulter Synchron LX20 analyzer (Beckman Coulter, Inc., Fullerton, CA): blood urea nitrogen (BUN), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), glucose, creatinine, total bilirubin, total protein, albumin, cholesterol, triglycerides, sodium, potassium, chloride, calcium and inorganic phosphorous. Total bile acids were to be determined on Study Days 15 and 29 only. Globulin and albumin/globulin ratio were calculated from the data.

   Hematology and clinical chemistry analytical results were recorded using electronic data capture (LABCAT, IPA Inc., Princeton, NJ, version 4.43).

7. Bone Marrow Micronucleus Assay: At the terminal and recovery necropsies, three bone marrow smears from the femur of the respective scheduled necropsy rats in Groups 1-3 were prepared for *in vivo* mutagenicity assessment (micronuclei determination). Slides were fixed in absolute methanol for 5 minutes and air-dried. The slides were stained with acridine orange and were examined under a fluorescent microscope for the presence of micronuclei. Polychromatic erythrocytes (PCE) stained orange and normochromatic erythrocytes (NCE) stained green. Micronuclei

appear as yellow spots. Approximately 2000 PCE were scored from each animal to detect frequency of micronuclei. In addition, to detect the toxicity of the test article to bone marrow, a total of 1000 erythrocytes were examined from each animal and the ratios were expressed as the percentage: PCE ÷ [PCE (including PCE with micronuclei) + NCE (including NCE with micronuclei)] x 100. Group 4 male rats (5 for each necropsy day) provided positive control evaluation. On the day prior to necropsy (Study Days 14 and 28), Group 4 males were injected intravenously with the positive control, cyclophosphamide, at a dose level of 30 mg/kg using a dose volume of 2 ml/kg body weight. These animals were discarded without further necropsy following removal of the femur and obtaining the bone marrow.

8. Necropsy: All animals in Groups 1-3 scheduled for necropsy at treatment termination (10/sex/group) and following recovery (5/sex/group) were fasted overnight, weighed, bled for clinical pathology, euthanized by CO_2 asphyxiation and subjected to a complete necropsy on Study Days 15 and 29, respectively. Necropsy included examination of the external surface of the body; all orifices; the cranial, thoracic and abdominal cavities and their contents. The following tissues were collected at necropsy and fixed in 10% neutral buffered formalin: adrenal glands, bone (femur), bone marrow (femur, in addition to that removed for micronucleus assessment), brain, cecum, colon, duodenum, epididymides, esophagus, eyes, gross lesions, harderian gland, heart, ileum, jejunum, kidneys, liver, lungs (infused with formalin), lymph nodes (mandibular and mesenteric), mammary gland (when present in regular abdominal skin section), ovaries, pancreas, parathyroid glands, pituitary gland, salivary glands (mandibular, sublingual and parotid), sciatic nerve, skeletal muscle, skin (injection site), spinal cord, spleen, stomach (forestomach and glandular), testes, thymus, thyroid glands, trachea, urinary bladder and uterus. Bone marrow was removed from the femur and a smear was prepared per standard operating procedures.

   Prior to fixing, the following tissues were weighed at necropsy: adrenal glands, brain, heart, kidneys, liver, ovaries, spleen, testes and thymus. To prevent possible tissue damage associated with weighing, the thyroid glands and parathyroid glands were weighed together after approximately 24 hours of formalin fixation. Paired organs were weighed together. Data were used to calculate organ-to-body weight ratios.

9. Histopathologic Evaluation: Tissues collected from animals in the vehicle control and high-dose group sacrificed on Study Day 15 were processed for histopathological evaluation. Sections of all tissues collected were cut approximately 5 microns thick, stained with hematoxylin and eosin and evaluated microscopically by a board-certified veterinary pathologist. All lesions were categorized either as drug-related or non-drug-related. Each lesion was listed and coded by the most specific topographic and morphologic diagnoses, severity and distribution using the Pathology Terminology Guidelines of the Toxicology Data Management System (TDMS) for the National Toxicology Program (July, 1992).

G. Statistical Procedures: Statistical comparisons for body weights, body weight gains, clinical chemistry, hematology, FOB (body temperature, foot splay, grip strength and body weight), micronuclei and organ weights were performed using analysis of variance (ANOVA) followed, where appropriate, by the *post hoc* Dunnett's test for comparing multiple treatment groups to a single control group via LABCAT software, Systat 10.2 software (Systat Software, Inc., Point Richmond, CA) and/or SigmaStat 2.03 software (Systat Software, Inc., Point Richmond, CA; formerly SPSS, Inc, Chicago, IL). Prior to comparison, the bone marrow micronucleus data [*i.e.*, micronucleated PCE (MPCE)] were transformed by adding one to each count and then taking the log of the adjusted count. A minimum significance level of $p \leq 0.05$ ($p < 0.05$ for LABCAT) was used in all comparisons.

H. Archives: All raw data and a copy of the final report will be retained in the IITRI archives for a period of one year from the date of completion of the study. At that time, the Sponsor will be consulted concerning the final disposition of the archival materials.

III. RESULTS

A. Dose Formulation Analysis: Results of the concentration, homogeneity and stability analyses of the dosing formulations are presented in Table 2 of Appendix B (page B-5) and discussed herein. As expected, the test article was not detected in any of the vehicle control dose formulation samples. Analysis of the low-dose test article dose formulations showed that the samples were within 10% of the target concentration of 0.015 mg/ml (concentration range of approximately 0.014-0.016 mg/ml; 92-108% of target), with the exception of one sample that had a concentration of approximately 0.012 mg/ml (80% of target). Three of the five high-dose test article dose formulation samples were within

10% of the target concentration of 0.030 mg/ml (concentration range of approximately 0.027-0.029; 91-96% of target); the remaining two samples had concentrations of approximately 0.017 or 0.039 mg/ml (55% or 129% of target, respectively). Thus, the majority of the test article formulation samples were within the 90-110% of the target concentration; it is unclear why some of the concentrations from both the low- and high-dose test article formulations were outside this range. For both dose levels, the formulations were not homogeneous [relative standard deviation (R.S.D.) > 10%]. The mean ± standard deviation concentration for the low-dose test article homogeneity samples was 0.014 ± 0.0018 mg/ml (~93% of target; R.S.D. = 13%) and the mean ± standard deviation concentration for the high-dose test article homogeneity samples was 0.024 ± 0.0067 mg/ml (~80% of target; R.S.D. = 28%). For both the low- and high-dose test article homogeneity samples, one of the samples was low [*e.g.*, the "top" portion sample (approximately 0.012 mg/ml) from low-dose test article formulation and the "bottom" portion sample (approximately 0.017 mg/ml) from the high-dose test article formulation]. If these low test article homogeneity samples are excluded, the mean ± standard deviation concentrations for the low- and high-dose test article formulations are approximately 0.015 ± 0.0013 mg/ml (~100% of target; R.S.D. = 9%) and 0.028 ± 0.0012 mg/ml (~93% of target; R.S.D. = 4%), respectively. Stability analyses showed that the both the low- and high-dose test article formulations were unstable when stored at room temperature (protected from light) for a minimum of seven days; however, since each test article formulation was prepared fresh daily, the instability of the test article is of little concern for this study.

B. Mortality and Clinical Observations: Clinical observations are summarized in Table 2, and individual animal data are presented in Appendix C, Table C-1. Figure 1 provides a guide to the clinical observation locations and severities noted in Appendix C, Table C-1. No animals died during the study. No drug-related adverse clinical signs were observed. Eye trauma was observed across all dose groups on Study Days 14, 16, 22 and/or 28 and was considered consequent to the retro-orbital blood collection method and unrelated to treatment with the test article. An ulcerated lesion was observed in one high-dose male on Study Day 28 which was considered incidental and unrelated to treatment with the test article.

C. Body Weights and Body Weight Gains: Body weights and body weight gains are summarized in Tables 3 and 4, respectively, and individual animal data are presented in

Appendix C, Tables C-2 and C-3, respectively. Additional body weight data, determined as part of the FOB, are summarized in Table 5 and individual animal data are presented in Appendix C, Table C-6. No statistically significant effects on mean body weight were observed in study animals during the treatment or recovery periods. Mean body weight gain was statistically significantly reduced in high-dose females on Study Day 8 of the treatment period, as compared to the vehicle control group. However, this result was thought to be incidental and unrelated to treatment with the test article, since it was an isolated occurrence. Thus, there were no treatment-related effects on mean body weight gains.

D. Functional Observational Battery (FOB): FOB tests for body temperatures, foot splay, forelimb and hindlimb grip strength and body weights are summarized in Table 5, and individual animal FOB tests for body temperatures, foot splay, forelimb and hindlimb grip strength and body weights and all other FOB observations are presented in Appendix C, Tables C-4 and C-6. A key for interpreting the individual animal FOB observations is also included in Appendix C, Table C-5. Mean body temperature was statistically significantly increased (as compared to the vehicle control group) in the low-dose males at pretest; however, since this occurred prior to dosing, it was considered incidental and unrelated to treatment. Mean body temperature was statistically significantly decreased (as compared to the vehicle control group) in the high-dose males on Study Day 14. Since the percentage difference from the vehicle control group was minimal (approximately 2%), this mean body temperature decrease is probably not toxicologically significant. In contrast to Study Day 14, mean body temperature was statistically significant increased (as compared to the vehicle control group) in the high-dose males on Study Day 28, which was probably an incidental occurrence that is probably not toxicologically meaningful. No effects on mean body temperature were observed in females throughout the study. No effects on mean foot splay were observed. Forelimb grip strength was statistically significantly increased in the low-dose males at pretest (as compared to the vehicle control group) and was considered unrelated to treatment because the difference was observed prior to dosing initiation. No effects on forelimb grip strength were observed in females throughout the study. Hindlimb grip strength was statistically significantly increased (as compared to the vehicle control group) in the high-dose females on Study Day 14. This effect may be related to treatment; however, since this effect was no longer observed on Study Day 28 (*i.e.*, recovered), it is probably not a

toxicologically significant finding. No other effects on hindlimb grip strength were observed throughout the study. No effects were observed for body weights collected on the day prior to the FOB evaluations (Study Day -2; pretest) or for body weights collected on the day FOBs were performed (Study Days 14 and 28). Visual examination of the individual FOB observation data (*i.e.*, remaining non-numerical FOB endpoints) did not reveal any noteworthy changes in the test article-treated animals at any time point.

E. Clinical Chemistry: Clinical chemistry data are summarized in Table 6, and individual animal data are presented in Appendix C, Table C-7. Blood urea nitrogen (BUN) levels were statistically significantly decreased in the low- and high-dose (non-fasted) females on Study Day 8, as compared to the control group. In contrast, BUN levels (as compared to the respective vehicle control groups) on Study Day 15 were statistically significantly increased in the low-dose (non-fasted) females, and were unaffected by treatment in the low- and high-dose (fasted) females and in the high-dose (non-fasted) females. The fact that the effects on BUN levels were opposite each other on Study Days 8 and 15, a dose-response relationship was not observed on Study Day 15 and the effects were no longer observed at the end of the recovery period on Study Day 29 suggests that these effects are of minimal toxicological significance. Serum albumin levels (as compared to the vehicle control group) on Study Day 15 were statistically significantly decreased in the low-dose (fasted) females and non-statistically significantly decreased in the high-dose (fasted) females. Cholesterol levels were statistically significantly increased on Study Day 15 in the low- and high-dose (non-fasted) males, as compared to the vehicle control group, whereas cholesterol levels on Study Day 15 in the low- and high-dose (fasted) males were similar to the vehicle control levels. The fact that cholesterol levels were no longer increased in the low- and high-dose (fasted) males (as compared to the vehicle control group) at the end of the recovery period suggests that the effect was transient and is probably not toxicologically significant. Triglyceride levels were statistically significantly increased (as compared to the vehicle control group) in the high-dose (fasted) males on Study Day 15 and non-statistically significantly increased in the low-dose (fasted) males. Since a dose-related increase was observed in serum triglyceride levels, this effect may be treatment-related; however, the fact that this effect was no longer observed at the end of the recovery period suggests that this may be of minimal toxicological significance. Thus, no consistent pattern of treatment-related,

toxicologically significant or dose-related effects was apparent and these changes were not considered drug-related. No other clinical chemistry effects were observed.

F. Hematology: Hematology data are summarized in Table 8, and individual animal data are presented in Appendix C, Table C-8. On Study Day 8 (as compared to the vehicle control group), red blood cell and relative large unstained cell counts were statistically significantly increased and relative reticulocyte counts were statistically significantly decreased in the low- and high-dose (non-fasted) males. The absolute large unstained cell count was also statistically significantly increased on Study Day 8 in the high-dose (non-fasted) males, with a non-statistically significant increase in the low-dose (non-fasted) males, as compared to the vehicle control group. On Study Day 15 (as compared to the vehicle control group), red blood cell count was statistically significantly increased in the low-dose (fasted) males and non-statistically increased in the high-dose (fasted) males, and the absolute and relative monocyte counts were statistically significantly increased in the low- and high-dose (fasted) males. The fact that each of these effects was no longer observed at the end of the recovery period (Study Day 29) suggests that these effects are transient and probably not toxicologically relevant. A statistically significant decrease in mean corpuscular volume and a statistically significant increase in mean corpuscular hemoglobin concentration were observed on Study Day 15 in the low-dose (fasted) males, as compared to the vehicle control group. Since dose-response relationships were not observed and the percentage differences from control were minimal (<3%), these effects were considered incidental and unrelated to treatment with the test article. A statistically significant decrease in the relative eosinophil count was observed at the end of the recovery period in the low-dose (fasted) females, as compared to the vehicle control group; however, since a dose-response relationship was not observed, this decrease is probably incidental and unrelated to treatment with the test article. No other hematology effects were observed.

G. Bone Marrow Micronucleated Erythrocytes: Bone marrow micronucleus data are summarized in Table 8 and individual animal data are presented in Appendix C, Table C-9. There were no statistically significant effects observed in treated rats of either sex on Study Day 15. Positive control males, as anticipated, showed statistically significantly increased MPCE [*i.e.*, log(MPCE+1] and statistically significantly decreased percent polychromatic erythrocyte (%PCE) count on Study Day 15, as compared to the vehicle control group. These results served to validate the assay. Since there was no apparent

test article-related effect on *in vivo* mutagenicity, bone marrow slides that were prepared from the Recovery animals on Study Day 29 were not evaluated (per Protocol).

H. Organ Weights: Absolute and relative (*i.e.*, organ-to-body weight ratios) organ weights are summarized in Tables 9 and 10, respectively, and individual animal data are presented in Appendix C, Tables C-10 and C-11, respectively. There were no statistically significant effects on male mean absolute organ weights on either Study Day 15 or 29 and there were no statistically significant effects on male mean relative organ weights on Study Day 15. Statistically significant increases (as compared to the vehicle control group) in mean absolute and relative adrenals weights were observed on Study Day 15 in low-dose females; however, these effects are probably incidental and unrelated to treatment with the test article since no dose-response relationships were observed. On Study Day 29 (as compared to the vehicle control group), mean relative heart weight was statistically significantly decreased by 10% in the low-dose males (with a non-statistically significant decrease of 7% in the high-dose males) and the mean absolute and relative heart weights were statistically significantly decreased by 8 or 9% in the high-dose females, respectively. The fact that these decreases were not observed at the end of the treatment period on Study Day 15 and that these findings were not correlated to any histologic findings (as discussed in the next section below) suggests that these findings were not associated with test article treatment. Consequently, all the observed organ weight effects were not considered toxicologically significant and/or not associated with test article treatment. No other organ weight effects were observed.

I. Gross Necropsy: Gross necropsy findings are summarized in a Pathology Report that is included as Appendix D. All of the gross lesions observed at necropsy were interpreted as incidental findings typically present in rat toxicology studies.

J. Histopathology: A detailed Pathology Report is included as Appendix D. All microscopic findings were interpreted as incidental findings that are commonly present in rat toxicology studies.

IV. DISCUSSION AND CONCLUSIONS

Intravenous administration of combined CuATSM/H_2ATSM (NSC-D729307) at targeted dose levels of 0.075 mg/kg/day (low-dose) or 0.150 mg/kg/day (high dose) for 14 consecutive days did not result in any clearly dose-related, treatment-related and/or toxicologically significant effects on mortality, clinical observations, mean body weights, mean body weight

gains, clinical chemistry, hematology, neurotoxicity (as measured by FOB), mutagenicity (bone marrow micronucleated erythrocytes) or organ weights. Finally, no treatment-related gross or microscopic lesions were observed in any of the tissues evaluated.

In conclusion, based on these findings, the no-observed-adverse-effect level (NOAEL) for this study was 0.150 mg/kg/day of CuATSM/H_2ATSM.

V. QUALITY ASSURANCE STATEMENT

Study Title: 14-Day Toxicity Study of CuATSM / H_2ATSM (NSC-D729307) in Rats

Project Number: 2073-002-002

Study Director: Thomas L. Horn, Ph.D.

The portions of this study conducted by IITRI have been subjected to inspections and the report has been audited by the IITRI Quality Assurance Unit in accordance with the Food and Drug Administration's "Good Laboratory Practice Regulations" – "CFR Title 21 Section 58.35." The report describes the methods and procedures used in the study and the reported results accurately reflect the raw data.

The following are the inspection dates and the dates inspection findings were reported:

	Findings Reported To:	
Inspection Dates	Study Director	Management
May 3, 2004	May 3, 2004	May 5, 2004
May 6, 2004	May 6, 2004	May 13, 2004
May 19, 2004	May 20, 2004	May 27, 2004
June 3, 2004	June 3, 2004	June 9, 2004
June 3, 2004	June 3, 2004	June 9, 2004
July 26, 2004	July 26, 2004	July 28, 2004
August 25-27, 30-31, September 1-3, 7-8, 10, 13-16, 2004	September 16, 2004	October 4, 2004
September 29, 2004	September 29, 2004	September 29, 2004
September 29, October 1, 4, 2004	October 4, 2004	October 4, 2004

12-14-04

Glenn B. Miller, M.S., C.Q.M. Date
Manager, Quality Assurance

VI. TABLES

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Table 1

List of Abbreviations

ALB	-	albumin (grams / deciliter serum)
A/G Ratio	-	albumin / globulin ratio
ALP	-	alkaline phosphatase (international units / liter serum)
ALT	-	alanine aminotransferase (international units / liter serum)
AST	-	aspartate aminotransferase (international units / liter serum)
#BASO	-	absolute basophil count (thousands / microliter blood)
%BASO	-	relative basophil count (percent)
BUN	-	blood urea nitrogen (milligrams nitrogen / deciliter serum)
CALC	-	calcium (milligrams / deciliter serum)
CHOL	-	cholesterol (milligrams / deciliter serum)
CL	-	chloride (millimoles / liter serum)
CRE	-	creatinine (milligrams / deciliter serum)
CuATSM	-	Copper-diacetyl-bis(N^4-methylthiosemicarbazone)
dL	-	deciliter
#EOS	-	absolute eosinophil count (thousands / microliter blood)
%EOS	-	relative eosinophil count (percent)
F	-	female
fL	-	femtoliter
g	-	grams
GLOB	-	globulin (grams / deciliter serum)
GLUC	-	glucose (milligrams / deciliter serum)
H_2ATSM	-	Diacetyl-bis(N^4-methylthiosemicarbazone)
HCT	-	hematocrit (percent)
HGB	-	hemoglobin (grams / deciliter blood)
IU	-	international units
K	-	potassium (millimoles / liter serum)
Kg or kg	-	kilograms
L	-	liter
#LUC	-	absolute large unstained cell count (thousands / microliter blood)
%LUC	-	relative large unstained cell count (percent)
#LYMPH	-	absolute lymphocyte count (thousands / microliter blood)
%LYMPH	-	relative lymphocyte count (percent)
M	-	male
MCH	-	mean corpuscular hemoglobin (picograms)
MCHC	-	mean corpuscular hemoglobin concentration (grams / deciliter blood)
MCV	-	mean corpuscular volume (femtoliter)
µL or uL	-	microliter
µmol	-	micromoles
mg	-	milligram
mL	-	milliliter
mmol	-	millimoles
#MONO	-	absolute monocyte count (thousands / microliter blood)
%MONO	-	relative monocyte count (percent)

Table 1 (cont.)

List of Abbreviations

MPCE	-	micronucleated polychromatic erythrocytes
N	-	number
NA	-	sodium (millimoles / liter serum)
#NEUT	-	absolute neutrophil count (thousands / microliter blood)
%NEUT	-	relative neutrophil count (percent)
NOAEL	-	no-observed-adverse-effect level
P or p	-	probability
PCE	-	polychromatic erythrocytes
pg	-	picogram
PLT	-	platelet count (thousands / microliter blood)
RBC	-	red blood cell count (millions of cells / microliter blood)
#RETIC	-	absolute reticulocyte count (billions of cells / liter blood)
%RETIC	-	relative reticulocyte count (percent)
SD or S.D.	-	standard deviation
TBIL	-	total bilirubin (milligrams / deciliter serum)
TG	-	triglycerides (milligrams / deciliter serum)
TP	-	total protein (grams protein / deciliter serum)
WBC	-	white blood cell count (thousands of cells / microliter blood)
x10e3 or x10.e3	-	thousand
x10e6	-	million
x10e9	-	billion

Table 2

SUMMARY OF OBSERVATION FREQUENCY@

STUDY: 2073002 SEX: MALE

DOSE:(mg/kg)	0	0.075	0.150
GROUP:	1-M	2-M	3-M
Recovery Sacrifice	5	5	5
Terminal Sacrifice	10	10	10
Normal	15	15	15
Lesion - ulcerated	0	0	1
Eye Trauma Due To Bleed	2	1	1
Total Number of Animals	15	15	15

SUMMARY OF OBSERVATION FREQUENCY@

STUDY: 2073002 SEX: FEMALE

DOSE:(mg/kg)	0	0.075	0.150
GROUP:	1-F	2-F	3-F
Recovery Sacrifice	5	5	5
Terminal Sacrifice	10	10	10
Normal	15	15	15
Eye Trauma Due To Bleed	2	3	2
Total Number of Animals	15	15	15

@ Frequency = number of animals exhibiting the sign at some point during the study

Table 3

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 2073002 SEX: MALE (TREATMENT PERIOD)

PERIOD	DOSE: (mg/kg) / GROUP:	0 / 1-M	0.075 / 2-M	0.150 / 3-M
DAY 1	MEAN	206	207	208
	S.D.	6.4	6.5	5.8
	N	15	15	15
DAY 5	MEAN	217	215	218
	S.D.	7.0	7.8	7.4
	N	15	15	15
DAY 8	MEAN	227	225	227
	S.D.	7.4	8.7	7.8
	N	15	15	15
DAY 12	MEAN	233	233	234
	S.D.	6.8	9.7	8.2
	N	15	15	15
DAY 14	MEAN	239	239	240
	S.D.	7.5	9.9	8.8
	N	15	15	15

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

Table 3 (cont.)

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 2073002 SEX: FEMALE (TREATMENT PERIOD)

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	0.075 2-F	0.150 3-F
DAY 1	MEAN	143	143	143
	S.D.	5.1	4.2	4.0
	N	15	15	15
DAY 5	MEAN	147	147	148
	S.D.	4.2	4.6	4.2
	N	15	15	15
DAY 8	MEAN	154	152	153
	S.D.	5.0	5.9	4.2
	N	15	15	15
DAY 12	MEAN	155	153	153
	S.D.	4.6	5.8	5.8
	N	15	15	15
DAY 14	MEAN	158	156	157
	S.D.	4.3	5.5	5.2
	N	15	15	15

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

Table 3 (cont.)

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 2073002 SEX: MALE (RECOVERY PERIOD)

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	0.075 2-M	0.150 3-M
DAY 15	MEAN	238	243	239
	S.D.	7.4	8.2	3.4
	N	5	5	5
DAY 19	MEAN	249	255	245
	S.D.	6.5	8.6	9.9
	N	5	5	5
DAY 22	MEAN	251	261	252
	S.D.	12.6	8.4	12.5
	N	5	5	5
DAY 26	MEAN	264	273	266
	S.D.	11.9	6.7	9.2
	N	5	5	5
DAY 28	MEAN	273	281	272
	S.D.	11.5	6.6	7.3
	N	5	5	5

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

Table 3 (cont.)

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 2073002 SEX: FEMALE (RECOVERY PERIOD)

PERIOD	DOSE: (mg/kg) / GROUP:	0 1-F	0.075 2-F	0.150 3-F
DAY 15	MEAN	159	160	155
	S.D.	3.3	7.1	7.0
	N	5	5	5
DAY 19	MEAN	165	164	159
	S.D.	6.6	9.9	8.3
	N	5	5	5
DAY 22	MEAN	167	166	161
	S.D.	7.2	9.1	9.1
	N	5	5	5
DAY 26	MEAN	171	171	167
	S.D.	7.2	8.8	8.1
	N	5	5	5
DAY 28	MEAN	173	173	172
	S.D.	8.4	9.4	8.4
	N	5	5	5

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

Table 4

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 2073002 SEX: MALE (TREATMENT PERIOD)

PERIOD	DOSE: (mg/kg) / GROUP:	0 1-M	0.075 2-M	0.150 3-M
DAY 5	MEAN	11	8	10
	S.D.	2.4	3.2	3.6
	N	15	15	15
DAY 8	MEAN	9	10	9
	S.D.	1.7	2.7	1.8
	N	15	15	15
DAY 12	MEAN	7	7	7
	S.D.	2.3	2.4	3.5
	N	15	15	15
DAY 14	MEAN	6	6	6
	S.D.	2.1	1.6	1.6
	N	15	15	15
TOTAL GAIN	MEAN	33	32	32
	S.D.	2.8	4.3	6.3
	N	15	15	15

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

Table 4 (cont.)

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 2073002 SEX: FEMALE (TREATMENT PERIOD)

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	0.075 2-F	0.150 3-F
DAY 5	MEAN	5	4	5
	S.D.	1.5	1.9	1.8
	N	15	15	15
DAY 8	MEAN	7	5	5*
	S.D.	1.9	2.2	2.2
	N	15	15	15
DAY 12	MEAN	1	0	0
	S.D.	2.8	2.1	3.3
	N	15	15	15
DAY 14	MEAN	3	4	4
	S.D.	1.9	1.8	1.9
	N	15	15	15
TOTAL GAIN	MEAN	16	13	14
	S.D.	2.9	3.7	2.9
	N	15	15	15

* P less than .05
** P less than .01

Analysis of Variance using DUNNETT'S Procedure

Table 4 (cont.)

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 2073002 SEX: MALE (RECOVERY PERIOD)

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	0.075 2-M	0.150 3-M
DAY 15	MEAN	1	2	1
	S.D.	2.1	2.4	1.4
	N	5	5	5
DAY 19	MEAN	11	12	6
	S.D.	5.5	1.9	8.5
	N	5	5	5
DAY 22	MEAN	3	6	7
	S.D.	10.7	2.2	3.2
	N	5	5	5
DAY 26	MEAN	13	12	15
	S.D.	2.4	2.1	3.6
	N	5	5	5
DAY 28	MEAN	9	7	6
	S.D.	1.4	1.1	2.5
	N	5	5	5
TOTAL GAIN@	MEAN	36	40	34
	S.D.	6.9	2.6	6.3
	N	5	5	5

* P less than .05 Analysis of Variance using DUNNETT'S Procedure
** P less than .01
@ Total Gain for Days 15-28

Table 4 (cont.)

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 2073002 SEX: FEMALE (RECOVERY PERIOD)

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	0.075 2-F	0.150 3-F
DAY 15	MEAN	-1	1	0
	S.D.	1.1	2.3	0.9
	N	5	5	5
DAY 19	MEAN	6	4	4
	S.D.	3.7	5.3	3.4
	N	5	5	5
DAY 22	MEAN	2	2	2
	S.D.	0.7	1.2	1.3
	N	5	5	5
DAY 26	MEAN	4	5	6
	S.D.	1.9	1.8	2.2
	N	5	5	5
DAY 28	MEAN	3	3	4
	S.D.	2.4	1.3	1.1
	N	5	5	5
TOTAL GAIN@	MEAN	14	15	16
	S.D.	5.8	2.2	3.2
	N	5	5	5

* P less than .05 Analysis of Variance using DUNNETT'S Procedure
** P less than .01
@ Total Gain for Days 15-28

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Table 5

Summary of Functional Observational Battery Tests

Body Temperature Data

Male Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (°C)	Study Day 14 (°C)	Study Day 28 (°C)
1	Mean	34.9	34.3	33.5
Vehicle Control	SD	0.61	0.34	0.61
(0.000 mg/kg/day)	N	10	10	5
2	Mean	35.6 *	34.1	33.7
(0.075 mg/kg/day)	SD	0.63	0.46	0.27
	N	10	10	5
3	Mean	35.3	33.6 *	35.1 *
(0.150 mg/kg/day)	SD	0.29	0.31	0.40
	N	10	10	5

Female Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (°C)	Study Day 14 (°C)	Study Day 28 (°C)
1	Mean	35.7	35.2	35.5
Vehicle Control	SD	0.60	0.77	0.85
(0.000 mg/kg/day)	N	10	10	5
2	Mean	35.8	35.1	34.6
(0.075 mg/kg/day)	SD	0.70	0.75	0.52
	N	10	10	5
3	Mean	36.0	35.4	35.8
(0.150 mg/kg/day)	SD	0.47	0.61	0.23
	N	10	10	5

* Statistically significant difference as compared to Vehicle Control (Group 1), $P \leq 0.05$

Table 5 (cont.)

Summary of Functional Observational Battery Tests

Foot Splay Data

Male Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (cm)	Study Day 14 (cm)	Study Day 28 (cm)
1	Mean	4.5	6.1	5.6
Vehicle Control	SD	0.76	0.59	0.52
(0.000 mg/kg/day)	N	10	10	5
2	Mean	4.7	6.1	6.3
(0.075 mg/kg/day)	SD	0.72	0.71	0.81
	N	10	10	5
3	Mean	4.5	5.5	4.5
(0.150 mg/kg/day)	SD	0.39	0.71	1.13
	N	10	10	5

Female Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (cm)	Study Day 14 (cm)	Study Day 28 (cm)
1	Mean	3.7	4.3	4.2
Vehicle Control	SD	0.51	0.68	0.45
(0.000 mg/kg/day)	N	10	10	5
2	Mean	3.8	4.6	4.5
(0.075 mg/kg/day)	SD	0.87	0.73	1.07
	N	10	10	5
3	Mean	4.3	4.4	4.1
(0.150 mg/kg/day)	SD	0.75	0.96	0.91
	N	10	10	5

Table 5 (cont.)

Summary of Functional Observational Battery Tests

Forelimb Grip Strength Data

Male Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
1	Mean	660	792	753
Vehicle Control	SD	65.7	92.3	78.2
(0.000 mg/kg/day)	N	10	10	5
2	Mean	727 *	834	733
(0.075 mg/kg/day)	SD	61.3	56.4	77.5
	N	10	10	5
3	Mean	701	792	738
(0.150 mg/kg/day)	SD	44.8	101.5	116.6
	N	10	10	5

Female Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
1	Mean	568	521	535
Vehicle Control	SD	41.5	103.8	119.0
(0.000 mg/kg/day)	N	10	10	5
2	Mean	576	601	589
(0.075 mg/kg/day)	SD	43.8	101.4	102.2
	N	10	10	5
3	Mean	585	622	558
(0.150 mg/kg/day)	SD	67.5	73.1	95.0
	N	10	10	5

* Statistically significant difference as compared to Vehicle Control (Group 1), $P \leq 0.05$

Table 5 (cont.)

Summary of Functional Observational Battery Tests

Hindlimb Grip Strength Data

Male Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
1	Mean	644	818	708
Vehicle Control	SD	109.8	153.2	72.1
(0.000 mg/kg/day)	N	10	10	5
2	Mean	746	681	678
(0.075 mg/kg/day)	SD	133.7	124.6	101.7
	N	10	10	5
3	Mean	727	856	558
(0.150 mg/kg/day)	SD	100.1	200.5	153.1
	N	10	10	5

Female Dose Group (CuATSM/H_2ATSM)		Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
1	Mean	563	497	495
Vehicle Control	SD	93.9	96.2	130.7
(0.000 mg/kg/day)	N	10	10	5
2	Mean	567	513	502
(0.075 mg/kg/day)	SD	135.2	127.3	142.2
	N	10	10	5
3	Mean	634	663 *	563
(0.150 mg/kg/day)	SD	113.1	182.7	59.0
	N	10	10	5

* Statistically significant difference as compared to Vehicle Control (Group 1), $P \leq 0.05$

Table 5 (cont.)

Summary of Functional Observational Battery Tests

Body Weight Data

Male Dose Group (CuATSM/H_2ATSM)		Study Day -2 (Pre-Study) [a] (g)	Study Day 14 (g)	Study Day 28 (g)
1	Mean	199	238	273
Vehicle Control	SD	5.0	6.6	11.5
(0.000 mg/kg/day)	N	10	10	5
2	Mean	200	239	281
(0.075 mg/kg/day)	SD	4.5	8.4	6.6
	N	10	10	5
3	Mean	200	236	272
(0.150 mg/kg/day)	SD	5.2	3.9	7.3
	N	10	10	5

Female Dose Group (CuATSM/H_2ATSM)		Study Day -2 (Pre-Study) [a] (g)	Study Day 14 (g)	Study Day 28 (g)
1	Mean	142	158	173
Vehicle Control	SD	4.5	4.2	8.4
(0.000 mg/kg/day)	N	10	10	5
2	Mean	142	157	173
(0.075 mg/kg/day)	SD	4.5	6.3	9.4
	N	10	10	5
3	Mean	142	155	172
(0.150 mg/kg/day)	SD	4.1	5.4	8.4
	N	10	10	5

[a] Body weights were inadvertently not collected on the day FOB evaluations were performed (*i.e.*, Study Day -1); pre-study body weight data were collected on Study Day -2.

Table 6

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE
STUDY NO: 2073022

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	145	5.2	97	366	56	84	0.32	17	0.4
SD	1.2	0.11	1.8	24.9	11.7	14.4	0.050	1.5	0.03
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	145	5.3	97	372	49	84	0.34	17	0.4
SD	1.0	0.25	2.3	22.9	2.5	16.6	0.039	1.3	0.03
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	145	5.3	97	375	54	84	0.34	18	0.4
SD	1.3	0.24	1.2	26.1	15.0	19.2	0.079	1.5	0.05
N	10	10	10	10	10	10	10	10	10

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE
STUDY NO: 2073022

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	GLUC	TP	ALB	GLOB	A/G RATIO	CHOL	TG	CALC	PHOS
UNITS:	mg/dL	g/dL	g/dL	g/dL	-	mg/dL	mg/dL	mg/dL	mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	133	5.8	4.0	1.8	2.2	40	128	11.1	11.5
SD	8.4	0.13	0.07	0.14	0.19	4.2	21.9	0.16	0.39
N	10	10	10	10	10	10	10	10	10
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	135	5.8	4.0	1.8	2.3	42	130	11.2	11.8
SD	11.6	0.16	0.16	0.10	0.18	3.4	27.6	0.19	0.50
N	10	10	10	10	10	10	10	10	10
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	135	5.9	4.0	1.9	2.2	41	133	11.2	11.6
SD	14.1	0.18	0.13	0.13	0.17	3.9	25.6	0.25	0.78
N	10	10	10	10	10	10	10	10	10

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE
STUDY NO: 2073022

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	146	4.8	98	321	44	76	0.33	17	0.4
SD	1.0	0.25	1.7	25.0	4.0	11.5	0.054	1.5	0.05
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	145	4.8	99	316	41	80	0.34	15*	0.4
SD	1.4	0.28	2.1	26.0	3.5	15.3	0.082	1.4	0.04
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	145	4.7	99	318	44	79	0.32	15*	0.4
SD	1.0	0.24	1.6	18.5	1.8	9.4	0.053	1.2	0.16
N	10	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE
STUDY NO: 2073022

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	GLUC	TP	ALB	GLOB	A/G RATIO	CHOL	TG	CALC	PHOS
UNITS:	mg/dL	g/dL	g/dL	g/dL	-	mg/dL	mg/dL	mg/dL	mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	134	5.5	3.9	1.6	2.4	55	87	10.9	11.1
SD	9.5	0.16	0.11	0.14	0.24	7.7	15.2	0.22	0.69
N	10	10	10	10	10	10	10	10	10
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	133	5.5	3.8	1.7	2.3	55	80	10.8	11.1
SD	8.9	0.23	0.10	0.20	0.31	3.5	10.7	0.18	0.62
N	10	10	10	10	10	10	10	10	10
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	134	5.5	3.8	1.7	2.3	53	76	10.9	11.2
SD	9.0	0.11	0.11	0.11	0.19	3.4	15.6	0.22	0.77
N	10	10	10	10	10	10	10	10	10

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	143	4.8	96	241	45	86	0.16	11	0.5
SD	1.3	0.18	1.4	12.6	1.7	2.3	0.055	0.8	0.09
N	5	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	142	4.6	97	226	46	88	0.14	11	0.5
SD	1.2	0.22	0.8	8.2	7.9	15.7	0.084	1.0	0.08
N	5	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	143	5.0	95	251	49	90	0.14	11	0.5
SD	1.8	0.27	1.5	20.0	4.3	7.3	0.054	2.5	0.05
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	143	5.1	95	345	49	78	0.12	15	0.4
SD	1.1	0.17	0.5	11.4	8.6	8.3	0.097	1.4	0.05
N	5	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	143	5.2	95	354	54	86	0.11	16	0.4
SD	0.8	0.18	2.0	22.4	14.9	15.5	0.058	1.5	0.05
N	5	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	142	5.2	95	344	55	87	0.14	15	0.4
SD	1.3	0.31	1.5	18.3	9.0	11.7	0.061	1.7	0.05
N	5	5	5	5	5	5	5	5	5

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

TEST(s): / UNITS:	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	124	5.8	3.9	1.9	2.1	32	46	10.7	10.4
SD	6.8	0.13	0.09	0.13	0.18	3.7	13.5	0.12	0.43
N	5	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	120	5.8	3.9	1.9	2.1	32	69	10.6	10.4
SD	8.0	0.04	0.04	0.07	0.11	2.9	15.7	0.12	0.21
N	5	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	117	6.0	4.0	2.0	2.1	34	76*	10.9	10.9
SD	2.2	0.14	0.08	0.08	0.05	4.0	15.5	0.23	0.43
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

TEST(s): / UNITS:	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	131	5.9	4.0	1.9	2.1	36	141	11.3	10.5
SD	8.7	0.19	0.13	0.13	0.14	1.3	13.2	0.11	0.58
N	5	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	134	5.9	4.0	1.9	2.1	39*	150	11.4	10.9
SD	3.8	0.14	0.04	0.13	0.13	1.3	19.3	0.11	0.28
N	5	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	142	5.9	4.0	1.9	2.1	39*	163	11.4	10.8
SD	26.2	0.11	0.05	0.14	0.18	1.8	40.4	0.24	0.61
N	5	5	5	5	5	5	5	5	5

* Significant Difference from Control $P \leq 0.05$

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	142	4.5	100	182	40	91	0.22	13	0.4
SD	1.6	0.37	2.4	16.2	4.0	19.6	0.072	2.8	0.04
N	5	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	142	4.6	100	185	38	82	0.17	13	0.4
SD	1.7	0.13	1.3	10.3	2.4	4.7	0.101	2.2	0.00
N	5	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	142	4.4	100	181	41	85	0.18	13	0.4
SD	1.7	0.16	2.2	17.5	5.9	5.4	0.025	1.8	0.07
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	141	4.7	98	292	36	71	0.17	14	0.4
SD	1.1	0.24	1.6	20.2	1.9	2.3	0.029	2.3	0.04
N	5	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	141	4.6	100	323	38	74	0.16	17*	0.4
SD	1.9	0.25	1.1	25.9	3.1	4.7	0.060	2.3	0.00
N	5	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	141	4.8	100	284	39	79	0.12	14	0.4
SD	1.8	0.52	1.5	42.7	5.3	7.4	0.055	1.4	0.00
N	5	5	5	5	5	5	5	5	5

* Significant Difference from Control $P \leq 0.05$

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

TEST(s): / UNITS:	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	101	5.8	4.0	1.8	2.3	46	35	10.5	8.8
SD	10.4	0.12	0.08	0.08	0.11	5.0	7.0	0.13	0.53
N	5	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	114	5.6	3.9*	1.8	2.2	44	39	10.5	9.5
SD	8.6	0.04	0.09	0.09	0.17	1.9	8.8	0.13	0.75
N	5	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	105	5.7	3.9	1.8	2.2	43	35	10.5	9.1
SD	4.1	0.13	0.10	0.16	0.24	3.3	10.8	0.17	0.61
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

TEST(s): / UNITS:	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	135	5.6	3.8	1.8	2.2	49	61	10.9	9.7
SD	6.5	0.16	0.09	0.13	0.15	4.0	13.6	0.15	0.70
N	5	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	127	5.8	3.9	1.9	2.1	47	84	11.0	10.0
SD	9.8	0.28	0.23	0.18	0.26	2.8	23.6	0.13	0.75
N	5	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	146	5.4	3.6	1.8	2.1	45	73	11.0	10.3
SD	12.4	0.24	0.15	0.13	0.15	3.4	14.6	0.19	0.96
N	5	5	5	5	5	5	5	5	5

* Significant Difference from Control $P \leq 0.05$

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE
STUDY NO: 2073022

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	143	4.9	99	172	42	81	0.41	13	0.4
SD	1.7	0.42	3.2	6.2	2.7	6.1	0.071	1.6	0.04
N	5	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	144	4.8	99	160	44	83	0.39	13	0.4
SD	1.7	0.30	2.0	19.1	5.6	5.8	0.040	2.0	0.04
N	5	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	145	4.9	99	155	41	81	0.42	12	0.4
SD	2.4	0.39	2.5	7.3	4.4	3.0	0.092	1.2	0.00
N	5	5	5	5	5	5	5	5	5

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE
STUDY NO: 2073022

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	GLUC	TP	ALB	GLOB	A/G RATIO	CHOL	TG	CALC	PHOS
UNITS:	mg/dL	g/dL	g/dL	g/dL	-	mg/dL	mg/dL	mg/dL	mg/dL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	124	5.9	4.1	1.8	2.2	24	56	10.5	10.0
SD	6.9	0.11	0.13	0.13	0.21	2.6	15.7	0.20	0.40
N	5	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	128	5.9	4.1	1.8	2.2	26	83	10.7	10.2
SD	9.8	0.28	0.23	0.11	0.15	3.2	23.6	0.12	0.72
N	5	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	114	5.8	4.0	1.9	2.2	25	61	10.6	10.0
SD	9.1	0.21	0.27	0.47	0.56	2.8	28.6	0.25	0.36
N	5	5	5	5	5	5	5	5	5

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE
STUDY NO: 2073022

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	NA	K	CL	ALP	ALT	AST	TBIL	BUN	CRE
UNITS:	mmol/L	mmol/L	mmol/L	IU/L	IU/L	IU/L	mg/dL	mg/dL	mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	145	4.7	100	125	44	90	0.39	14	0.4
SD	1.8	0.15	1.5	13.3	17.0	29.8	0.040	1.5	0.00
N	5	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	145	5.0	100	130	37	79	0.44	13	0.4
SD	2.1	0.17	1.8	6.4	3.5	2.7	0.078	1.6	0.07
N	5	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	145	5.0	101	133	39	81	0.43	14	0.4
SD	1.0	0.38	1.3	16.6	4.1	4.9	0.064	1.9	0.00
N	5	5	5	5	5	5	5	5	5

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	GLUC	TP	ALB	GLOB	A/G RATIO	CHOL	TG	CALC	PHOS
UNITS:	mg/dL	g/dL	g/dL	g/dL	-	mg/dL	mg/dL	mg/dL	mg/dL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
MEAN	107	5.8	3.9	1.9	2.1	41	17	10.5	9.6
SD	5.4	0.08	0.11	0.16	0.27	1.9	2.2	0.23	0.33
N	5	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM									
MEAN	102	5.7	4.0	1.8	2.3	40	21	10.5	9.8
SD	9.5	0.16	0.15	0.09	0.15	2.3	5.3	0.26	0.94
N	5	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM									
MEAN	107	5.7	3.8	1.9	2.1	39	13	10.4	9.8
SD	3.7	0.19	0.15	0.11	0.16	2.6	3.3	0.23	0.75
N	5	5	5	5	5	5	5	5	5

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (μmol/L)

Fasted Males

PERIOD(s):	Day 15	Day 29
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
MEAN	22.1	21.1
SD	3.69	3.42
N	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM		
MEAN	18.2	20.8
SD	1.17	4.68
N	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM		
MEAN	19.9	20.7
SD	3.82	8.25
N	5	5

Non-Fasted Males

PERIOD(s):	Day 15	Day 29
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
MEAN	12.1	NA
SD	1.83	NA
N	5	0
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM		
MEAN	12.1	NA
SD	2.98	NA
N	5	0
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM		
MEAN	14.2	NA
SD	6.40	NA
N	5	0

NA – not applicable

Table 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (µmol/L)

Fasted Females

PERIOD(s):	Day 15	Day 29
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
MEAN	18.5	21.8
SD	3.68	7.18
N	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM		
MEAN	17.6	20.8
SD	3.90	4.27
N	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM		
MEAN	16.6	28.0
SD	0.83	11.51
N	5	5

Non-Fasted Females

PERIOD(s):	Day 15	Day 29
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
MEAN	21.8	NA
SD	13.76	NA
N	5	0
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM		
MEAN	10.7	NA
SD	5.45	NA
N	5	0
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM		
MEAN	17.5	NA
SD	12.88	NA
N	5	0

NA – not applicable

Table 7

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
UNITS:	x10e3/uL	x10e6/uL	g/dL	%	fL	pg	g/dL	x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	12.16	8.45	15.2	47.9	56.6	18.0	31.9	827
SD	0.821	0.171	0.20	1.27	0.71	0.38	0.89	42.5
N	10	10	10	10	10	10	10	10
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	11.88	8.69*	15.4	48.8	56.2	17.8	31.6	788
SD	0.701	0.272	0.38	1.72	0.74	0.18	0.55	99.2
N	10	10	10	10	10	10	10	10
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	12.37	8.70*	15.4	48.9	56.2	17.7	31.6	829
SD	0.662	0.204	0.27	1.28	0.71	0.31	0.65	44.0
N	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	3.0	255.6	16.8	79.7	2.2	0.5	0.6	0.3
SD	0.32	24.24	2.57	2.60	0.59	0.16	0.13	0.10
N	10	10	10	10	10	10	10	10
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	2.7*	233.2	16.6	79.3	2.6	0.6	0.6	0.4*
SD	0.23	20.38	2.35	2.61	0.47	0.18	0.11	0.10
N	10	10	10	10	10	10	10	10
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	2.7*	236.5	15.4	80.6	2.3	0.7	0.6	0.4*
SD	0.26	22.79	2.58	3.08	0.53	0.39	0.19	0.07
N	10	10	10	10	10	10	10	10

*-Significant Difference from Control P < .05

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC
UNITS:	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	2.05	9.67	0.27	0.07	0.07	0.03
SD	0.419	0.499	0.072	0.021	0.019	0.007
N	10	10	10	10	10	10
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	1.98	9.41	0.31	0.07	0.07	0.04
SD	0.350	0.497	0.059	0.022	0.016	0.009
N	10	10	10	10	10	10
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	1.91	9.97	0.29	0.09	0.08	0.04**
SD	0.348	0.624	0.070	0.048	0.027	0.008
N	10	10	10	10	10	10

**-Significant Difference from Control P < .01

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
UNITS:	x10e3/uL	x10e6/uL	g/dL	%	fL	pg	g/dL	x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	11.42	8.35	15.2	46.9	56.1	18.2	32.4	806
SD	0.719	0.268	0.45	1.09	0.86	0.20	0.49	87.3
N	10	10	10	10	10	10	10	10
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	11.00	8.19	15.0	46.0	56.2	18.3	32.7	745
SD	0.655	0.467	0.91	2.55	0.83	0.42	0.47	89.1
N	10	10	10	10	10	10	10	10
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	11.52	8.36	15.3	46.9	56.0	18.3	32.6	730
SD	1.342	0.241	0.35	1.56	0.66	0.32	0.75	52.9
N	10	10	10	10	10	10	10	10

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	2.2	181.3	15.4	80.1	2.7	0.6	0.7	0.4
SD	0.34	25.03	3.06	3.27	0.55	0.20	0.10	0.07
N	10	10	10	10	10	10	10	10
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	2.3	189.1	17.3	78.5	2.5	0.7	0.7	0.3
SD	0.22	15.46	4.14	3.69	0.63	0.18	0.17	0.12
N	10	10	10	10	10	10	10	10
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	2.2	182.0	16.0	79.6	2.6	0.8	0.7	0.3
SD	0.23	19.44	3.18	3.32	0.72	0.19	0.16	0.07
N	10	10	10	10	10	10	10	10

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC
UNITS:	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	1.75	9.16	0.31	0.07	0.08	0.05
SD	0.311	0.851	0.060	0.025	0.009	0.010
N	10	10	10	10	10	10
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	1.91	8.62	0.28	0.07	0.08	0.04
SD	0.560	0.400	0.069	0.018	0.019	0.014
N	10	10	10	10	10	10
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	1.84	9.17	0.30	0.09	0.08	0.04
SD	0.452	1.135	0.081	0.019	0.016	0.009
N	10	10	10	10	10	10

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
UNITS:	x10e3/uL	x10e6/uL	g/dL	%	fL	pg	g/dL	x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	9.75	8.25	14.7	47.0	57.0	17.8	31.1	876
SD	0.617	0.229	0.34	1.33	0.91	0.27	0.29	36.9
N	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	10.58	8.57*	15.1	47.7	55.6*	17.6	31.7*	900
SD	0.519	0.135	0.14	0.44	0.38	0.11	0.21	39.9
N	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	10.87	8.53	15.0	48.3	56.7	17.6	31.0	842
SD	1.131	0.165	0.27	1.20	1.05	0.29	0.28	93.4
N	5	5	5	5	5	5	5	5

Non-Fasted Males

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
UNITS:	x10e3/uL	x10e6/uL	g/dL	%	fL	pg	g/dL	x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	10.78	8.22	14.5	47.1	57.2	17.6	30.8	906
SD	1.060	0.379	0.59	2.39	0.30	0.17	0.40	65.7
N	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	10.86	8.26	14.7	47.5	57.5	17.8	30.9	879
SD	0.722	0.311	0.41	1.68	0.25	0.41	0.60	24.1
N	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	11.51	8.45	14.7	48.5	57.4	17.4	30.4	880
SD	1.383	0.299	0.48	1.97	0.58	0.29	0.62	25.6
N	5	5	5	5	5	5	5	5

* Significant Difference from Control $P \leq 0.05$

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	#EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	4.6	380.2	20.0	76.9	1.5	0.9	0.5	0.2
SD	0.34	24.57	3.43	3.59	0.33	0.53	0.09	0.05
N	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	4.4	375.7	20.6	75.3	2.3*	1.1	0.4	0.3
SD	0.34	26.99	1.08	1.16	0.49	0.22	0.04	0.08
N	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	4.5	379.1	17.9	78.3	2.3*	0.7	0.5	0.3
SD	0.54	39.06	1.29	1.65	0.52	0.15	0.15	0.11
N	5	5	5	5	5	5	5	5

Non-Fasted Males

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	#EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	5.0	408.7	17.6	78.2	3.0	0.6	0.4	0.3
SD	0.35	38.27	1.97	1.82	0.55	0.09	0.04	0.15
N	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	4.7	388.3	18.3	77.9	2.6	0.4	0.4	0.3
SD	0.12	20.69	2.15	2.01	0.23	0.11	0.10	0.11
N	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	4.8	408.1	16.4	80.1	2.3	0.6	0.4	0.2
SD	0.98	91.78	1.85	2.12	0.34	0.14	0.07	0.11
N	5	5	5	5	5	5	5	5

* Significant Difference from Control $P \leq 0.05$

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

TEST(s): / UNITS:	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	1.95	7.49	0.15	0.09	0.04	0.02
SD	0.379	0.515	0.033	0.048	0.009	0.005
N	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	2.18	7.97	0.24*	0.12	0.04	0.03
SD	0.206	0.300	0.057	0.023	0.008	0.008
N	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	1.93	8.51	0.26*	0.08	0.05	0.04
SD	0.144	0.939	0.070	0.020	0.022	0.016
N	5	5	5	5	5	5

Non-Fasted Males

TEST(s): / UNITS:	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	1.90	8.41	0.32	0.06	0.05	0.04
SD	0.349	0.713	0.078	0.012	0.009	0.013
N	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	1.99	8.47	0.28	0.05	0.04	0.04
SD	0.258	0.613	0.018	0.016	0.011	0.013
N	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	1.91	9.20	0.27	0.07	0.05	0.03
SD	0.453	0.867	0.076	0.017	0.008	0.012
N	5	5	5	5	5	5

* Significant Difference from Control $P \leq 0.05$

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

TEST(s): / UNITS:	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	8.74	7.68	14.2	44.3	57.6	18.6	32.2	855
SD	1.826	0.485	0.94	3.37	1.07	0.47	0.65	53.4
N	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	10.56	8.03	14.8	46.9	58.4	18.4	31.5	931
SD	1.483	0.324	0.47	1.44	1.23	0.18	0.51	105.2
N	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	10.01	8.02	14.8	46.8	58.4	18.4	31.6	950
SD	0.630	0.207	0.21	1.03	1.76	0.36	0.46	117.2
N	5	5	5	5	5	5	5	5

Non-Fasted Females

TEST(s): / UNITS:	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	9.66	7.54	13.9	44.7	59.3	18.4	31.0	950
SD	0.465	0.345	0.68	2.46	1.27	0.18	0.43	143.2
N	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	9.77	7.82	14.5	46.0	58.8	18.5	31.5	884
SD	0.865	0.210	0.08	1.59	0.59	0.40	0.93	103.8
N	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	9.79	7.44	13.8	43.9	59.2	18.6	31.4	958
SD	1.227	0.503	0.72	2.53	0.80	0.54	0.84	122.8
N	5	5	5	5	5	5	5	5

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	#EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	5.3	404.0	21.3	75.6	1.8	0.6	0.4	0.3
SD	0.69	39.34	9.25	9.88	0.68	0.08	0.11	0.11
N	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	5.8	464.4	18.6	77.8	2.0	0.8	0.4	0.4
SD	1.08	80.40	1.58	1.76	0.67	0.15	0.11	0.08
N	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	5.4	427.9	16.8	79.9	1.9	0.8	0.3	0.2
SD	1.04	78.83	2.52	2.63	0.42	0.29	0.05	0.11
N	5	5	5	5	5	5	5	5

Non-Fasted Females

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	#EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	5.3	396.7	15.9	80.9	1.8	0.5	0.5	0.4
SD	0.67	59.03	2.26	2.59	0.58	0.15	0.15	0.26
N	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	4.6	363.0	15.4	81.3	1.9	0.7	0.4	0.3
SD	0.42	24.45	2.13	2.83	0.79	0.11	0.11	0.11
N	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	5.5	405.4	19.7	76.6	2.6	0.5	0.3	0.3
SD	1.39	77.60	5.25	5.90	0.94	0.08	0.07	0.05
N	5	5	5	5	5	5	5	5

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

TEST(s):	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC
UNITS:	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	1.74	6.74	0.15	0.05	0.03	0.02
SD	0.267	1.985	0.028	0.013	0.015	0.013
N	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	1.97	8.22	0.20	0.08	0.04	0.04
SD	0.333	1.202	0.072	0.015	0.009	0.011
N	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	1.69	8.00	0.18	0.08	0.04	0.03
SD	0.312	0.499	0.040	0.029	0.005	0.009
N	5	5	5	5	5	5

Non-Fasted Females

TEST(s):	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC
UNITS:	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	1.53	7.83	0.18	0.05	0.05	0.03
SD	0.153	0.609	0.055	0.015	0.009	0.026
N	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	1.50	7.96	0.19	0.07	0.04	0.03
SD	0.237	0.815	0.067	0.008	0.013	0.011
N	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	1.95	7.47	0.26	0.05	0.03	0.03
SD	0.650	0.899	0.115	0.010	0.013	0.005
N	5	5	5	5	5	5

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
UNITS:	x10e3/uL	x10e6/uL	g/dL	%	fL	pg	g/dL	x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	11.04	8.75	15.3	48.2	55.2	17.4	31.5	987
SD	0.990	0.791	1.62	3.44	1.19	0.56	1.42	330.4
N	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	11.87	9.07	15.8	49.5	54.6	17.4	31.8	886
SD	0.194	0.316	0.51	2.01	0.64	0.14	0.57	25.7
N	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	10.87	8.87	15.2	48.7	55.0	17.2	31.3	986
SD	1.753	0.717	1.05	3.07	1.15	0.22	0.36	244.2
N	5	5	5	5	5	5	5	5

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	3.2	270.4	20.1	76.0	2.3	0.6	0.4	0.5
SD	1.91	125.89	2.62	2.79	0.43	0.21	0.04	0.18
N	5	5	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	2.2	203.1	20.6	75.3	2.5	0.8	0.3	0.5
SD	0.27	26.64	2.31	2.66	0.60	0.16	0.13	0.11
N	5	5	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	2.9	251.4	21.8	73.9	2.7	0.6	0.3	0.7
SD	1.68	113.42	5.05	5.72	0.72	0.14	0.13	0.15
N	5	5	5	5	5	5	5	5

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC
UNITS:	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL
Group: 1-M : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	2.21	8.40	0.26	0.07	0.04	0.06
SD	0.305	0.835	0.070	0.028	0.008	0.020
N	5	5	5	5	5	5
Group: 2-M : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	2.45	8.94	0.29	0.10	0.04	0.06
SD	0.275	0.358	0.067	0.019	0.013	0.018
N	5	5	5	5	5	5
Group: 3-M : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	2.44	7.97	0.30	0.07	0.03	0.07
SD	0.974	0.808	0.110	0.015	0.013	0.031
N	5	5	5	5	5	5

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	WBC	RBC	HGB	HCT	MCV	MCH	MCHC	PLT
UNITS:	x10e3/uL	x10e6/uL	g/dL	%	fL	pg	g/dL	x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	9.65	8.28	15.7	48.2	58.3	18.9	32.5	791
SD	1.545	0.635	1.15	3.22	0.65	0.21	0.43	117.6
N	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	9.95	8.24	15.5	48.1	58.4	18.9	32.3	846
SD	0.741	0.191	0.25	1.14	0.62	0.25	0.62	103.6
N	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	9.04	8.36	15.8	49.0	58.6	18.9	32.2	875
SD	1.153	0.306	0.36	1.58	1.15	0.63	0.69	84.2
N	5	5	5	5	5	5	5	5

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	%RETIC	#RETIC	%NEUT	%LYMPH	%MONO	%EOS	%BASO	%LUC
UNITS:	%	x10e9/L	%	%	%	%	%	%
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
MEAN	2.6	206.7	25.4	70.5	2.3	1.0	0.4	0.5
SD	1.80	118.66	4.29	4.55	0.59	0.18	0.09	0.13
N	5	5	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM								
MEAN	1.9	151.2	19.4	76.8	2.1	0.6*	0.4	0.7
SD	0.05	6.56	2.96	3.40	0.60	0.13	0.11	0.15
N	5	5	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM								
MEAN	1.7	142.1	20.4	75.3	2.6	0.7	0.4	0.6
SD	0.15	11.85	5.66	5.66	0.75	0.23	0.19	0.19
N	5	5	5	5	5	5	5	5

*-Significant Difference from Control P < .05

Table 7 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	#NEUT	#LYMPH	#MONO	#EOS	#BASO	#LUC
UNITS:	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL	x10e3/uL
Group: 1-F : 0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
MEAN	2.48	6.77	0.22	0.09	0.04	0.05
SD	0.748	0.825	0.073	0.034	0.011	0.019
N	5	5	5	5	5	5
Group: 2-F : 0.075 mg/kg/day CuATSM / H2ATSM						
MEAN	1.93	7.64	0.21	0.06	0.04	0.07
SD	0.330	0.713	0.054	0.013	0.007	0.011
N	5	5	5	5	5	5
Group: 3-F : 0.150 mg/kg/day CuATSM / H2ATSM						
MEAN	1.84	6.81	0.24	0.07	0.03	0.06
SD	0.493	1.038	0.084	0.021	0.019	0.019
N	5	5	5	5	5	5

Table 8

Summary of Bone Marrow Polychromatic Erythrocyte (PCE) Data

Males – Day 15

Dose Group (CuATSM / H_2ATSM)		%PCE [a]	Micronucleated PCE (MPCE) (Number/2000 PCE Scored)	Log(MPCE+1) [b]
1	Mean	56.1	2	0.346
Vehicle Control	SD	13.78	1.8	0.2904
(0.00 mg/kg/day)	N	10	10	10
2	Mean	55.3	3	0.529
Low Dose	SD	9.36	1.3	0.1633
(0.075 mg/kg/day)	N	10	10	10
3	Mean	54.8	3	0.499
High Dose	SD	9.56	1.5	0.2257
(0.150 mg/kg/day)	N	10	10	10
4	Mean	32.7 *	15	1.169 *
Positive Control [c]	SD	10.51	5.5	0.1663
	N	5	5	5

[a] %PCE = [(PCE + MPCE) ÷ 1000 erythrocytes] × 100

[b] The counts of micronuclei for each animal were transformed by adding 1 to each count and then the log of the adjusted number was taken and used for statistical comparisons.

[c] Positive Control = Cyclophosphamide (30 mg/kg) injected intravenously approximately 24 hours before sacrifice

* Statistically significant difference as compared to Vehicle Control (Group 1), $P \leq 0.05$

Table 8 (cont.)

Summary of Bone Marrow Polychromatic Erythrocyte (PCE) Data

Females – Day 15

Dose Group (CuATSM / H_2ATSM)		%PCE [a]	Micronucleated PCE (MPCE) (Number/2000 PCE Scored)	Log(MPCE+1) [b]
1	Mean	52.8	3	0.516
Vehicle Control	SD	5.18	1.6	0.2008
(0.00 mg/kg/day)	N	10	10	10
2	Mean	55.7	2	0.451
Low Dose	SD	7.58	1.7	0.2347
(0.075 mg/kg/day)	N	10	10	10
3	Mean	49.6	3	0.554
High Dose	SD	9.23	1.4	0.1554
(0.150 mg/kg/day)	N	10	10	10

[a] %PCE = [(PCE + MPCE) ÷ 1000 erythrocytes] × 100

[b] The counts of micronuclei for each animal were transformed by adding 1 to each count and then the log of the adjusted number was taken and used for statistical comparisons.

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Table 9

Summary of Absolute Organ Weights

Males – Day 15

Dose Group (CuATSM/H_2ATSM mg/kg/day)		Absolute Organ Weight (g)								
		Adrenals	**Brain**	**Heart**	**Kidneys**	**Liver**	**Spleen**	**Testes**	**Thymus**	**Thyroids** [a]
1	Mean	0.056	1.83	0.90	1.98	8.90	0.53	2.92	0.281	0.019
Vehicle Control	SD	0.0098	0.036	0.071	0.095	0.766	0.039	0.072	0.0285	0.0032
(0.000)	N	10	10	10	10	10	10	10	10	10
2	Mean	0.057	1.83	0.87	1.97	9.14	0.51	2.94	0.311	0.016
Low Dose	SD	0.0071	0.056	0.035	0.122	1.036	0.040	0.106	0.0451	0.0040
(0.075)	N	10	10	10	10	10	10	10	10	10
3	Mean	0.052	1.82	0.91	1.95	8.99	0.54	2.89	0.279	0.015
High Dose	SD	0.0071	0.026	0.076	0.076	0.876	0.025	0.090	0.0246	0.0040
(0.150)	N	10	10	10	10	10	10	10	10	10

[a] Thyroids weighed with parathyroids

Table 9 (cont.)

Summary of Absolute Organ Weights

Females – Day 15

Dose Group (CuATSM/H_2ATSM mg/kg/day)		Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Thyroids [a]
1	Mean	0.058	1.71	0.66	1.31	5.11	0.081	0.39	0.275	0.015
Vehicle Control	SD	0.0054	0.047	0.066	0.049	0.299	0.0265	0.037	0.0315	0.0020
(0.000)	N	10	10	10	10	10	10	10	10	10
2	Mean	0.066*	1.72	0.63	1.30	5.15	0.080	0.41	0.280	0.012
Low Dose	SD	0.0073	0.038	0.033	0.052	0.322	0.0239	0.025	0.0380	0.0023
(0.075)	N	10	10	10	10	10	10	10	10	10
3	Mean	0.065	1.74	0.63	1.31	5.14	0.078	0.40	0.278	0.015
High Dose	SD	0.0094	0.037	0.037	0.089	0.326	0.0126	0.035	0.0258	0.0041
(0.150)	N	10	10	10	10	10	10	10	10	10

[a] Thyroids weighed with parathyroids

* Statistically significant difference from Vehicle Control (Group 1), $P \leq 0.05$

Table 9 (cont.)

Summary of Absolute Organ Weights

Males – Day 29

Dose Group (CuATSM/H_2ATSM mg/kg/day)		Absolute Organ Weight (g)								
		Adrenals	**Brain**	**Heart**	**Kidneys**	**Liver**	**Spleen**	**Testes**	**Thymus**	**Thyroids** [a]
1	Mean	0.056	1.86	1.03	1.94	8.04	0.57	2.91	0.302	0.019
Vehicle Control	SD	0.0114	0.048	0.069	0.101	0.441	0.071	0.308	0.0388	0.0018
(0.000)	N	5	5	5	5	5	5	5	5	5
2	Mean	0.057	1.86	0.98	1.96	8.16	0.55	3.10	0.309	0.023
Low Dose	SD	0.0058	0.070	0.053	0.105	0.488	0.027	0.110	0.0169	0.0038
(0.075)	N	5	5	5	5	5	5	5	5	5
3	Mean	0.053	1.89	0.98	1.94	8.34	0.56	3.11	0.305	0.023
High Dose	SD	0.0036	0.048	0.032	0.053	0.503	0.018	0.080	0.0413	0.0033
(0.150)	N	5	5	5	5	5	5	5	5	5

[a] Thyroids weighed with parathyroids

Table 9 (cont.)

Summary of Absolute Organ Weights

Females – Day 29

Dose Group (CuATSM/H_2ATSM mg/kg/day)		Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Thyroids [a]
1	Mean	0.058	1.76	0.72	1.28	5.53	0.073	0.41	0.272	0.017
Vehicle Control	SD	0.0053	0.021	0.038	0.072	0.972	0.0090	0.057	0.0271	0.0028
(0.000)	N	5	5	5	5	5	5	5	5	5
2	Mean	0.062	1.76	0.71	1.30	5.27	0.077	0.42	0.279	0.017
Low Dose	SD	0.0048	0.024	0.038	0.067	0.250	0.0068	0.026	0.0362	0.0050
(0.075)	N	5	5	5	5	5	5	5	5	5
3	Mean	0.053	1.75	0.66*	1.25	5.05	0.078	0.40	0.257	0.018
High Dose	SD	0.0037	0.043	0.033	0.077	0.368	0.0037	0.027	0.0363	0.0064
(0.150)	N	5	5	5	5	5	5	5	5	5

[a] Thyroids weighed with parathyroids

* Statistically significant difference from Vehicle Control (Group 1), $P \leq 0.05$

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Table 10

Summary of Organ-to-Body Weight Ratios

Males – Day 15

Dose Group (CuATSM/H_2ATSM mg/kg/day)		Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Thyroids [b]
1	Mean	228	0.025	0.80	0.39	0.87	3.90	0.23	1.28	0.123	0.008
Vehicle Control	SD	6.7	0.0038	0.018	0.026	0.023	0.269	0.013	0.031	0.0113	0.0013
(0.000)	N	10	10	10	10	10	10	10	10	10	10
2	Mean	226	0.025	0.82	0.39	0.87	4.04	0.23	1.31	0.138	0.007
Low Dose	SD	11.4	0.0033	0.040	0.016	0.035	0.307	0.013	0.065	0.0216	0.0018
(0.075)	N	10	10	10	10	10	10	10	10	10	10
3	Mean	229	0.023	0.80	0.40	0.85	3.92	0.24	1.27	0.122	0.007
High Dose	SD	11.0	0.0030	0.044	0.029	0.022	0.213	0.014	0.068	0.0107	0.0016
(0.150)	N	10	10	10	10	10	10	10	10	10	10

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Thyroids weighed with parathyroids

Table 10 (cont.)

Summary of Organ-to-Body Weight Ratios

Females – Day 15

Dose Group (CuATSM/H_2ATSM mg/kg/day)		Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Thyroids [b]
1	Mean	148	0.039	1.16	0.44	0.89	3.46	0.055	0.26	0.186	0.010
Vehicle Control	SD	5.1	0.0041	0.039	0.041	0.019	0.182	0.0183	0.024	0.0171	0.0014
(0.000)	N	10	10	10	10	10	10	10	10	10	10
2	Mean	145	0.046*	1.18	0.43	0.90	3.55	0.055	0.28	0.193	0.009
Low Dose	SD	4.0	0.0057	0.042	0.025	0.045	0.243	0.0166	0.020	0.0251	0.0016
(0.075)	N	10	10	10	10	10	10	10	10	10	10
3	Mean	148	0.044	1.18	0.43	0.88	3.47	0.053	0.27	0.188	0.010
High Dose	SD	4.6	0.0058	0.029	0.028	0.046	0.198	0.0076	0.019	0.0143	0.0027
(0.150)	N	10	10	10	10	10	10	10	10	10	10

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Thyroids weighed with parathyroids
* Statistically significant difference from Vehicle Control (Group 1), $P \leq 0.05$

Table 10 (cont.)

Summary of Organ-to-Body Weight Ratios

Males – Day 29

Dose Group (CuATSM/H_2ATSM mg/kg/day)		Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes	Thymus	Thyroids [b]
1	Mean	248	0.023	0.75	0.42	0.78	3.24	0.23	1.18	0.121	0.008
Vehicle Control	SD	12.0	0.0046	0.033	0.029	0.021	0.053	0.032	0.115	0.0126	0.0009
(0.000)	N	5	5	5	5	5	5	5	5	5	5
2	Mean	256	0.022	0.73	0.38*	0.76	3.18	0.21	1.21	0.121	0.009
Low Dose	SD	5.8	0.0022	0.017	0.020	0.023	0.132	0.009	0.035	0.0071	0.0016
(0.075)	N	5	5	5	5	5	5	5	5	5	5
3	Mean	249	0.021	0.76	0.39	0.78	3.34	0.22	1.24	0.122	0.009
High Dose	SD	8.9	0.0017	0.031	0.005	0.013	0.161	0.018	0.068	0.0129	0.0015
(0.150)	N	5	5	5	5	5	5	5	5	5	5

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Thyroids weighed with parathyroids
* Statistically significant difference from Vehicle Control (Group 1), $P \leq 0.05$

Table 10 (cont.)

Summary of Organ-to-Body Weight Ratios

Females – Day 29

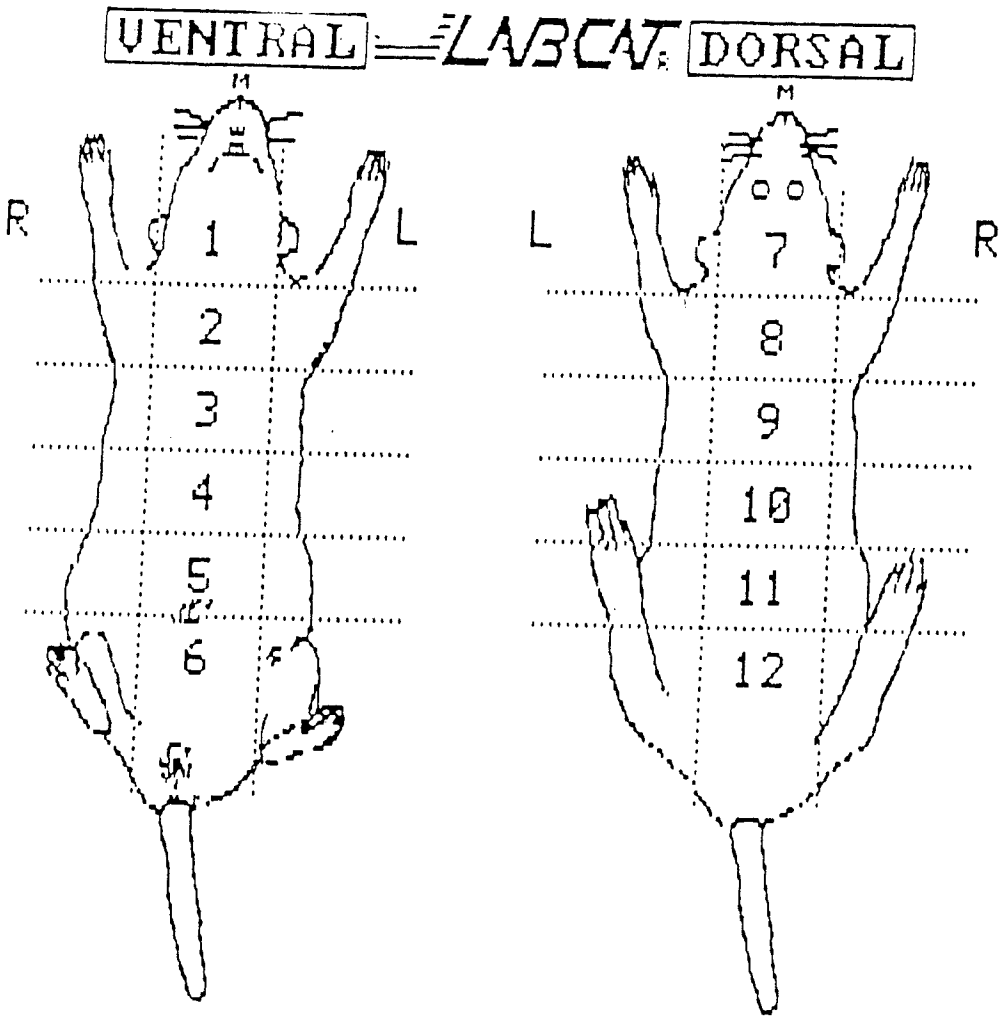
Dose Group (CuATSM/H_2ATSM mg/kg/day)		Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen	Thymus	Thyroids [b]
1	Mean	157	0.037	1.13	0.46	0.81	3.53	0.047	0.27	0.174	0.011
Vehicle Control	SD	7.1	0.0046	0.049	0.023	0.018	0.601	0.0057	0.032	0.0138	0.0022
(0.000)	N	5	5	5	5	5	5	5	5	5	5
2	Mean	158	0.039	1.12	0.45	0.82	3.33	0.048	0.26	0.176	0.011
Low Dose	SD	7.5	0.0019	0.041	0.027	0.042	0.176	0.0032	0.022	0.0214	0.0033
(0.075)	N	5	5	5	5	5	5	5	5	5	5
3	Mean	154	0.035	1.14	0.42*	0.81	3.27	0.050	0.26	0.166	0.012
High Dose	SD	7.8	0.0029	0.043	0.011	0.019	0.183	0.0045	0.008	0.0171	0.0038
(0.150)	N	5	5	5	5	5	5	5	5	5	5

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Thyroids weighed with parathyroids
* Statistically significant difference from Vehicle Control (Group 1), $P \leq 0.05$

VII. FIGURE

Figure 1

LABCAT Clinical Sign Location and Severity Guide
(see Appendix C, Table C-1)



Location Abbreviation Key: L = Left, M = Middle, R = Right

Severity Scale Key: 1 = minimal, 2 = mild, 3 = moderate, 4 = severe

VIII. APPENDICES

Appendix A: Protocol, Protocol Amendment and Protocol Deviation

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

SPONSOR:

Toxicology and Pharmacology Branch
Developmental Therapeutics Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
National Institutes of Health
Bethesda, Maryland 20892

PROJECT OFFICER: Elizabeth R. Glaze, Ph.D.

CONTRACT NUMBER: N01-CM-42202

CONTRACTOR:

IIT Research Institute (IITRI)
Life Sciences Group
10 West 35th Street
Chicago, IL 60616

IITRI PROJECT NO.: 2073-002-002

PRINCIPAL INVESTIGATOR: David L. McCormick, Ph.D., D.A.B.T.

STUDY DIRECTOR: Thomas L. Horn, Ph.D.

PROPOSED IN-LIFE PHASE:

Start: May 6, 2004 (Day 1)

Finish: June 3, 2004 (Day 29)

I. OBJECTIVE

The objective of this study is to determine target organ toxicity of CuATSM / H_2ATSM (NSC- D729307) and its reversibility given intravenously to rats once a day for 14 days.

II. MATERIALS AND METHODS

A. Test and Control Articles

1. Name of Test Article:

Copper-diacetyl-bis(N^4-methylthiosemicarbazone) / diacetyl-bis(N^4-methylthiosemicarbazone (CuATSM / H_2ATSM; NSC-D729307)

2. Name of Control Articles:

Dimethyl sulfoxide (DMSO)

Ethanol (100%)

Saline (0.9% sodium chloride)

Cyclophosphamide

3. Characterization and Documentation of Methods of Synthesis, Fabrication or Derivation:

a. Test Article:

Compound identity, strength, quality, stability and purity as well as documentation of methods of synthesis, fabrication or derivation are the responsibility of the NCI. Sufficient quantity of test article shall be reserved for archiving from each lot and shipment used.

b. Control Articles:

Characterization of the control articles may be attained by recording all pertinent information provided on the container labels or by retaining the container labels themselves as raw data.

4. Stability and Storage:

The test article will be stored in its original container at controlled room temperature (approximately 20 to 25°C), protected from light. Each bulk control article will be stored in its original container. The DMSO, 100% ethanol and saline control articles will be stored at controlled room temperature (approximately 20 to 25°C) and the cyclophosphamide control article will be stored refrigerated (approximately 2 to 8°C). The control articles are stable unopened through the date of expiration as provided by the manufacturer/supplier.

5. Formulation Preparation and Storage:

The test article will be dissolved in DMSO to produce a stock solution (approximately 10 mg/ml). The stock solution will be aliquotted and further diluted with DMSO (if necessary), and then 100% ethanol and saline will be added to produce a dosing solution with final concentrations of test article, DMSO, ethanol and saline of 0.015 or 0.030 mg/mL, 0.3% (v/v), 7% (v/v) and 92.7% (v/v), respectively. The test article stock solution and each test article dosing formulation will be prepared fresh daily. The vehicle control [0.3% (v/v) DMSO / 7% (v/v) ethanol / 92.7% (v/v) saline] will also be prepared daily. When not in use, the test article dosing formulations will be stored in the dark at room temperature (approximately 20 to 25°C).

Cyclophosphamide will be dissolved in saline. When not in use, the cyclophosphamide dosing formulation will be stored refrigerated (approximately 2 to 8°C).

6. Dose Concentration, Stability and Homogeneity Analyses:

Dose concentration, stability and homogeneity analyses will be performed by an analytical laboratory designated by the Sponsor. An adequate quantity of each test article and vehicle control dosing formulation used on Study Days 1, 8 and 14 will be obtained for dose concentration analyses and stored frozen. Similarly, an adequate quantity of each test article dosing formulation used on Study Day 1 (consisting of dose concentration analysis of a top, middle and bottom portion) will be obtained for homogeneity analyses and stored frozen. An adequate quantity from each test article dosing formulation used on Study Day 1 will also be obtained on Study Days 1, 8 and 14 for determination of stability and stored frozen. Samples will then be shipped (on dry ice) in an insulated container to the Sponsor-designated laboratory for analysis. The reporting of results will be the

responsibility of the Sponsor or Sponsor's designee and will not be included in IITRI's Final Report.

Dose formulation samples will not be obtained from the cyclophosphamide dosing formulation; thus, analyses for concentration, stability and homogeneity will not be performed.

B. Test System

1. Species, Sex, Strain Supplier and Test System Justification:

Approximately sixty male and fifty female Fischer 344 [CDF(F-344)/CrlBR] rats will be obtained from Charles River Laboratories (Raleigh, NC) for use in this study. This is an accepted strain and species to support studies of compounds used or intended for use in humans.

2. Initial Age and Weight:

Rats will be approximately 8 to 9 weeks old at arrival. At the time of receipt, male rats will weigh approximately 150 to 175 grams and female rats will weigh approximately 115 to 140 grams. On the first day of dosing, the weight range of rats will be approximately 200 to 250 grams (males) or 140 to 180 grams (females), and rats will be approximately 9 to 10 weeks of age.

3. Care and Housing:

Upon receipt, rats will be housed up to three per cage to facilitate acclimation to the automatic watering system. Prior to treatment initiation and throughout the treatment period, rats will be housed individually in stainless steel cages equipped with automatic watering systems. Absorbent cage boards will be placed underneath animal cages to contain liquid and solid wastes. Procedures for animal care and housing will be in accordance with the Guide for Care and Use of Laboratory Animals (National Research Council, 1996) and the U.S. Dept. of Agriculture through the Animal Welfare Act (Public Law 99-198).

Animal room temperatures will be monitored continuously using an automated system. Temperature and relative humidity will also be recorded manually each day. A 12-hour light/dark cycle (maintained with an automatic timer) will be used. Animal rooms will be held within a temperature range of approximately 18 to 26°C, and a humidity range of approximately 30 to 70%.

4. Diet and Water Supply:

Certified Rodent Diet #5002 (PMI Nutrition International, Brentwood, MO) will be provided *ad libitum* to all rats throughout the study, except for overnight fasts prior to scheduled necropsy. City of Chicago public drinking water from an automatic watering system will be provided *ad libitum* to all rats throughout the study. No contaminants will be present in the feed or water which could interfere and affect the results of the study. Analytical data from the lots of diet to be used in the study and water analysis records are retained on file at IITRI.

5. Quarantine:

All rats will be quarantined for a minimum of 7 days prior to dosing. During the quarantine period, each rat will receive a detailed physical examination to ensure its suitability as a test animal. No prophylactic or therapeutic treatment will be administered during the quarantine period. Only healthy animals will be placed on study.

6. Animal Identification:

Each study rat will be identified by metal ear tag bearing an animal number that is unique within the study. Each rat cage will be identified by Project Number, Group, Animal Number and Sex.

C. Experimental Design

1. Randomization:

In order to obtain groups that are comparable by weight, all rats will be randomly assigned to their respective treatment groups using a computer-based body weight stratification procedure. Individual body weights required for randomization will be determined during the quarantine period.

2. Group Assignments:

After randomization, 90 rats (15/sex/group) will be assigned to two test article dose groups and a vehicle control group (VCTL) as follows.

GROUP	DAILY DOSE CuATSM / H_2ATSM		# of Rats at Study Start (M + F)	# of Rats Sacrificed	
	mg/kg/day	mg/m²/day		Day 15 (M + F)	Day 29 (M + F)
1 (VCTL)	0.000	0.00	15 + 15	10 + 10	5 + 5
2	0.075	0.45	15 + 15	10 + 10	5 + 5
3	0.150	0.90	15 + 15	10 + 10	5 + 5
4	Cyclophosphamide (30 mg/kg)		10 + 0	5 + 0	5 + 0

Study animals will be dosed once daily for 14 consecutive days. Sixty study rats (10/sex/group) will be sacrificed on Study Day 15 (terminal necropsy) and the remaining study rats will then be observed for 15 days thereafter and will be sacrificed on Study Day 29 (recovery necropsy).

An additional group of ten male rats will be used as a positive control group for *in vivo* mutagenicity assessment. Five animals will receive an intravenous injection of cyclophosphamide (30 mg/kg) on Study Day 14, and will be euthanized approximately 18-24 hours after injection on Study Day 15. The remaining five animals will receive an intravenous injection of cyclophosphamide (30 mg/kg) on Study Day 28, and will be euthanized approximately 18-24 hours after injection on Study Day 29. Bone marrow smears will be prepared, processed and analyzed for the presence of micronuclei (see Section II.C.5.f.).

3. Route of Administration and Reason for Choice:

The test compounds will be given intravenously because this is the intended route of administration of these compounds in humans.

4. Dosing Procedure:

Starting on Study Day 1, each study rat in each test article dose group will receive a slow bolus intravenous injection of the test article once per day for 14 consecutive days; rats in the vehicle control group will receive an equivalent volume of vehicle once a day for 14 consecutive days. The amount of drug administered to each rat will be based on its most recent individual body weight. The initial dosing parameters will be entered into the computer program (e.g., dose level and dose volume for each animal) and will be checked by two individuals, one of whom is the Study Director, who will initial and date the verification.

To reduce the possibility of masking drug effects, a uniform volume of administration (5 mL/kg body weight/dose) will be selected and maintained constant for all rats in Groups 1-3. This will be done by making separate drug concentrations for each dose group, and varying dosing volumes to accommodate individual body weights. A uniform volume of administration (2 mL/kg body weight/dose) will also be used for rats in Group 4.

5. Measurements:

a. Moribundity/Mortality Observations:

During the quarantine period, all animals will be observed once daily for mortality or evidence of moribundity. Throughout the treatment period, all animals will be observed twice daily for mortality or evidence of moribundity. Any abnormal clinical signs will be recorded. Mortality/moribundity checks will be separated by a minimum of four hours.

b. Clinical Signs:

A detailed hand-held clinical and physical observation will be performed on all animals once during the quarantine period (pretest) and performed on all study animals in Groups 1-3 at least once weekly throughout the treatment and recovery periods. A cageside clinical observation will also be performed daily during the treatment period on all study rats in Groups 1-3 approximately 1 to 2 hours after dosing, and once daily thereafter during the recovery period, or more often as clinical signs warrant. Rat identification numbers, dose volumes, drug formulations, vehicle, clinical effects, day(s) of death, individual body weights as specified below and other pertinent information will be recorded.

c. Body Weight:

Animals will be weighed at receipt (random sample) and once during quarantine (at randomization). All surviving study rats in Groups 1-3 will be individually weighed on Study Days 1, 5, 8, 12, 15, and twice weekly during the recovery period. For all surviving study animals scheduled for terminal or recovery euthanasia in Groups 1-3, a final (non-fasted) body weight will be obtained on Study Days 14 or 28, respectively, and a final (fasted) body weight will be obtained on Study Days 15 or 29, respectively. When applicable, the rats should be weighed at approximately the same time each day. Body weights for

surviving animals in Group 4 will be collected on Day14 or Day 28 only. Body weights will also be measured on the day functional observational battery (FOB) evaluations are performed (see section II.C.5.d. below).

d. Functional Observational Battery (FOB):

The last ten (numerically) surviving study rats/sex/group in Groups 1-3 will be evaluated with a functional observational battery at baseline (Study Days -3 to -1; pre-study) and at the end of Week 2 (Study Day 14); all surviving study rats in Groups 1-3 will be evaluated at the end of Week 4 (Study Day 28; recovery animals). During the treatment period, these evaluations will occur approximately 2-4 hours after dosing. The following parameters will be assessed:

Home cage observation
Audition (click, startle)
Open field (mobility/gait)
Pupil response
Vision
Catalepsy
Righting reflex
Body weights
Handheld observation
Body temperature
Tail pinch
Eye blink response
Hindlimb extension
Grip strength
Foot splay

e. Clinical Pathology:

Blood will be drawn from the last ten (numerically) surviving study rats/sex/group in Groups 1-3 for clinical pathology determinations on Study Days 8 and 15. Blood will also be drawn from each surviving study rat in Groups 1-3 on Study Day 29. Blood will be taken from the retro-orbital plexus, except prior to sacrifice when blood may also be collected from the abdominal aorta, if necessary. A blood sample will be obtained prior to the necropsy of each study rat in Groups 1-3 sacrificed in a moribund condition.

<u>Hematology</u>:

Erythrocyte count (RBC)
Hemoglobin (HGB)
Hematocrit (HCT)
Mean corpuscular volume (MCV)
Mean corpuscular hemoglobin (MCH)
Mean corpuscular hemoglobin concentration (MCHC)
Platelet count (PLT)

Reticulocyte count (RETIC; absolute and relative)
Total leukocyte count (WBC)
Differential leukocyte count (absolute and relative)

Clinical Chemistry:

Blood urea nitrogen (BUN)
Serum aspartate aminotransferase (AST)
Serum alanine aminotransferase (ALT)
Alkaline phosphatase (ALP)
Serum glucose (GLU)
Creatinine (CREA)
Total bilirubin (TBIL)
Total protein (TP)
Albumin (ALB)
Globulin (GLOB; by calculation)
Albumin/Globulin (A/G) ratio
Cholesterol (CHOL)
Triglycerides (TG)
Sodium (NA)
Potassium (K)
Chloride (CL)
Calcium (CA)
Inorganic phosphorous (PO4)
Total bile acids (TBA; on Days 15 and 29 only)

f. Postmortem Procedure:

The first ten (numerically) surviving study rats/sex/group in Groups 1-3 will be sacrificed on Study Day 15 (terminal necropsy); surviving study rats in Groups 1-3 will be sacrificed on Study Day 29 (recovery necropsy). Rats in the positive control group (Group 4) will be euthanized on Study Day 15 after removal of the femur(s); Group 4 animals will be discarded without necropsy.

At scheduled necropsy, at least two bone marrow smears will be prepared from each study animal in Groups 1-3 for *in vivo* mutagenicity assessment (micronuclei determination). The slides will be fixed in 100% methanol, and slides from the Study Day 15 necropsy will be assessed for mutagenicity. If a mutagenic effect is found, the slides from the Study Day 29 necropsy (recovery animals) will be subsequently assessed for mutagenicity. On Study Day 15 or 29, at least two bone marrow smears will also be prepared, fixed in 100% methanol

and assessed for mutagenicity (where applicable) from rats treated with cyclophosphamide (Group 4).

Moribund study rats in Groups 1-3 will be terminated out of sequence with complete histopathology and clinical pathology performed as for scheduled necropsy. Study rats in Groups 1-3 found dead will have a complete necropsy, unless severely autolyzed. A necropsy will not be performed on study rats from Group 4 that are moribund or found dead.

All study rats in Groups 1-3 will have final (fasted) body weights taken and will be bled (if applicable) for clinical pathology determinations prior to termination. A complete necropsy and all antemortem observations will be recorded for each study rat in Groups 1-3 and commented on or confirmed at necropsy. Study rats in Groups 1-3 which are clinically normal will also be so indicated. A pathologist will be available to examine any unusual findings.

Prior to fixing, tissues from animals in Groups 1-3 from major organs on the list below marked with an asterisk (*) will be weighed (paired organs will be weighed together) at terminal or recovery necropsy. To prevent possible tissue damage associated with weighing, the thyroid and parathyroid glands (**) will be weighed together after a minimum of approximately 16-18 hours of formalin fixation (for animals surviving to terminal or recovery necropsy only).

The tissues (from animals in Groups 1-3) listed below will be examined, sampled and fixed in 10% neutral buffered formalin. The exceptions will be eyes with harderian gland which will be fixed in Davidson's fixative and the testes/epididymides which will be fixed in Bouin's fixative. The rat identification will be retained with tissues taken during necropsy.

* Adrenal glands (2)
  Bone (femur)
  Bone marrow (femur)
* Brain
  Cecum
  Colon
  Duodenum
  Epididymides
  Esophagus
  Eyes (2)
* Gonads - testes/ovaries (2)

Gross lesions
Harderian gland
* Heart
Ileum
Jejunum
* Kidneys (2)
* Liver
Lungs (infuse with formalin)
Lymph nodes (mandibular and mesenteric)
Mammary gland (when present in regular abdominal skin section)
Pancreas
** Parathyroid gland (when present in regular thyroid section)
Pituitary gland
Salivary glands [mandibular, sublingual, and parotid (when present in routine section)]
Sciatic nerve
Skeletal muscle
Skin (injection site)
Spinal Cord (thoracolumbar segment for routine section, or entire spinal cord if neurological signs indicate cord involvement)
* Spleen
Stomach (forestomach and glandular)
* Thymus
** Thyroid glands
Trachea
Urinary bladder
Uterus

g. Microscopic Pathology:

Sections of all tissues from the high dose and the vehicle control groups will be embedded, put into blocks, cut approximately 5 microns thick, stained with hematoxylin and eosin, and examined microscopically by a pathologist. Records of gross findings from postmortem observations will be available to the pathologist during histopathologic evaluations. All lesions will be categorized either as drug-related or non-drug-related. Each lesion will be listed and coded by the most specific topographic and morphologic diagnoses, severity and distribution using the Pathology Terminology Guidelines of the Toxicology Data Management System (TDMS) for the National Toxicology Program (July, 1992). Target tissues only will be assessed in the other test article-treated dose group at additional expense. Target

tissues in recovery animals will be evaluated only in the dose groups which demonstrated the lesions seen on Study Day 15, in addition to corresponding recovery control animals.

Bone marrow smears will be stained with acridine orange and the polychromatic erythrocytes will be evaluated for micronucleus frequency.

D. Statistical Analysis

Statistical analysis of continuous data (body weights, body weight gains, food consumption, clinical pathology, organ weights, etc.) will be performed using analysis of variance (ANOVA), with post-hoc comparisons made using Dunnett's test. The raw data on the counts of micronuclei for each animal will be transformed by adding 1 to each count and then taking the log of the adjusted number. The transformed micronucleus data will then be analyzed using ANOVA, with post-hoc comparisons made using Dunnett's test. A minimum significance level of $p \leq 0.05$ will be used for all comparisons.

III. QUALITY ASSURANCE

A. Type of Study

This is a nonclinical laboratory study and will require compliance with the FDA Good Laboratory Practice (GLP) Regulations. Data from this study will be included as part of a final report to be submitted to the FDA.

B. Standard Operating Procedures

All operations pertaining to this study, unless specifically defined in this protocol, will be performed according to the laboratory's Standard Operating Procedures. Any deviations will be documented.

C. Protocol Amendments

All changes in or revisions of an approved protocol and the reasons therefore will be documented, signed, and dated by the Principal Investigator, Study Director and the NCI Project Officer. Amendments will be maintained with the protocol. Verbal approval for changes in the protocol may be granted by the NCI Project Officer, but a written amendment will follow.

D. Records

Data will be audited by the IITRI Quality Assurance Unit. Study data will be archived in the IITRI archives for a period of one year from the date of completion of the study. At that time, the Sponsor will be contacted to

determine the final disposition of the archival materials. IITRI's Quality Assurance Unit will maintain a complete record of the disposition of all archival materials.

IV. REPORTING AND DISCUSSION OF DATA

A. Progress Reports

Non-GLP status reports summarizing the progress of the study will be provided at monthly intervals. These reports will detail the status of the study on the reporting date, any problems encountered and proposed means of resolution.

B. Final Report

The data and results of this study will be submitted as a separate draft report, due 40 working days after the last necropsy in this study. The final report will be due 15 working days after return of the draft report for revision.

This report will accurately and completely describe the study design, procedures and findings, present an analysis and summary of the data followed by the conclusions derived from the analyses. The report will also include: (a) a cover page which will include the title, contract number, authors, laboratory address, dates of initiation and completion, and sponsor; (b) an abstract to be placed at the beginning of the final report; (c) a comprehensive summary to be placed after the abstract; and (d) the signature of the Study Director and any others deemed necessary.

In order to maximize output in the final months of this contract, in lieu of a final study report, the contractor can submit an abbreviated study report. This abbreviated report will include: (a) a cover page which will include the title, contract number, authors, laboratory name and address, dates of initiation and completion, and sponsor; (b) a table of contents; (c) all individual animal data and appropriate summary tables for the following: mortality, body weights, clinical observations, hematology, clinical chemistry, necropsy gross findings, histopathology and any other pertinent data; and (d) the signature of the Study Director and any others deemed necessary. This abbreviated study report may not meet all the applicable GLP requirements (e.g., objectives, description of methods and test system, description of results, etc.).

In addition to the appropriate number of paper copies of the report, an Electronic Copy should also be submitted. The data should be copied to a CD-ROM disk preferably as a text-based Acrobat pdf file.

V. PROTOCOL APPROVALS

Study Director: Thomas J H 5/5/04 (Date)

Principal Investigator: D Miller 5/5/04 (Date)

NCI Project Officer: [signature] 5/6/04 (Date)

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

PROTOCOL AMENDMENT #1

I. NATURE OF REVISION

The analytical results for dose concentration, stability and homogeneity will be included in IITRI's Final Report; however, the methods used, data and the reporting of results will not be performed according to Good Laboratory Practice Regulations.

The formulation samples were shipped for analysis on June 1, 2004 to:

Dr. Ruiwen Zhang
Associate Professor
Department of Pharmacology and Toxicology
University of Alabama at Birmingham
1670 University Blvd., VH 124A
Birmingham, AL 35294-0019.

REASON FOR CHANGE: This change is at the request of the Sponsor.

II. PROTOCOL AMENDMENT APPROVALS

Study Director: Thomas L. Horn, Ph.D. — 7/26/04 (Date)

Principal Investigator: David L. McCormick, Ph.D., D.A.B.T. — 7/26/04 (Date)

NCI Project Officer: Elizabeth R. Glaze, Ph.D. — 8/14/04 (Date)

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

PROTOCOL DEVIATION #1

NATURE OF DEVIATION

Date of Deviation: July 30, 2004

Section IV.B. Final Report: A draft report was not submitted after 40 working days after the last necropsy in this study, as indicated in the Protocol.

EFFECT ON STUDY: This deviation is not expected to affect the integrity of the study.

Study Director: Thomas L. Horn, Ph.D. 9/29/04 (Date)

Appendix B: Dose Formulation Analysis Report, Test Article Data Sheets and Certificates of Analysis for Control Articles

SPECIAL REPORT

"Analysis of dose formulation samples of Cu-ATSM + H_2-ATSM (NSC 729307) submitted to UAB"

Accomplished as part of

WORK ASSIGNMENT # 12, Pharmacology Studies with a KSR Antisense Phosphorothioate Oligodeoxynucleotide (KSR AS-214231; NSC 731442), an Inhibitor of Ras Signaling

on

Contract N01-CM-07111

Preclinical Pharmacological Studies of Antitumor and Anti-HIV Agents

Submitted to: Dr. Joseph M. Covey, Project Officer

Submitted by:

Department of Pharmacology and Toxicology
University of Alabama at Birmingham
Birmingham, AL 35294-0019

Period of performance:

June 2004

Analysis of dose formulation samples of Cu-ATSM + H_2-ATSM (NSC 729307) submitted to UAB

Statement of work. As part of an effort in supporting preliminary toxicology studies with Cu-ATSM + H_2-ATSM (NSC 729307), we analyzed dose formulation samples from studies conducted by IITRI, another NCI contractor.

Analytical Method. The HPLC system consisted of a Hewlett Packard 1050 ChemStation with a UV detector (Agilent 1050 series). Determination of H_2-ATSM and Ni+Cu-ATSM was achieved using a Zorbax SB-18 (5 μm, 150×4.6 mm) analytical column with a LiChroCART 100 RP-18 guard column. The flow rate was 1 mL/min. The column elute was monitored by UV at 345 nm.

Peak areas were determined for quantification of H_2-ATSM and Ni+Cu-ATSM. Linear regression and correlation analysis were accomplished to establish the standard peak-area/concentration curves for H_2-ATSM and Ni+Cu-ATSM. This method, which was previously developed and validated, is described in more detail in Appendix A. Standard curves for H_2-ATSM and Ni+Cu-ATSM in aqueous solution are presented in Figure 1.

Analysis of samples .We analyzed dosing formulations sent to us by IITRI. The results are in Tables 1 and 2. For these tables, each number under "Conc. (ng/mL)" is intended to represent the total amount of "ATSM" (Cu-ATSM + Ni-ATSM + H_2-ATSM) in the sample. As determined by the derived data, there was no apparent problem with the analytical procedure, for duplicate analyses gave similar values. It also appears that there were no gross errors in dose preparation, for most of the samples supposedly containing 15 or 30 μg/mL contained about those amounts, as determined by measurement of the H_2-ATSM peak. It is not clear why quantitation using the Ni+Cu-ATSM curve was lower overall. At both concentrations, there were losses of compound in the stored samples (Day 8 and Day 14 Stability). The 15 μg/mL samples appeared to be more stable than the 30 μg/mL samples. This observation could be due to precipitation of the material, but we noted no precipitate.

CONTRIBUTING PERSONNEL

Ruiwen Zhang, M.D., Ph.D., DABT, Principal Investigator and Study Director
Donald L. Hill, Ph.D., Co-Principal Investigator
Hui Wang, M.D., Ph.D., Instructor, Laboratory Manager
Mao Li, M.D., Post-Doctoral Fellow

Figure 1. Standard Curves for ATSM and Ni+Cu-ATSM

Concentration	ATSM			Ni+ Cu ATSM		
(ng/mL)	Peak Area	Peak Area	Average	Peak Area	Peak Area	Average
0.00	0.000	0.000	0.00	0.000	0.000	0.00
5.00	0.086	0.069	0.08	0.028	0.014	0.02
10.00	0.204	0.153	0.18	0.141	0.115	0.13
25.00	0.915	0.788	0.85	0.284	0.288	0.29
50.00	2.003	1.974	1.99	0.518	0.595	0.56
100.00	4.078	4.034	4.06	0.988	1.120	1.05
250.00	10.439	10.307	10.37	2.542	2.559	2.55
500.00	20.553	19.864	20.21	5.074	5.162	5.12
1000.00	42.972	41.545	42.26	9.669	9.661	9.67

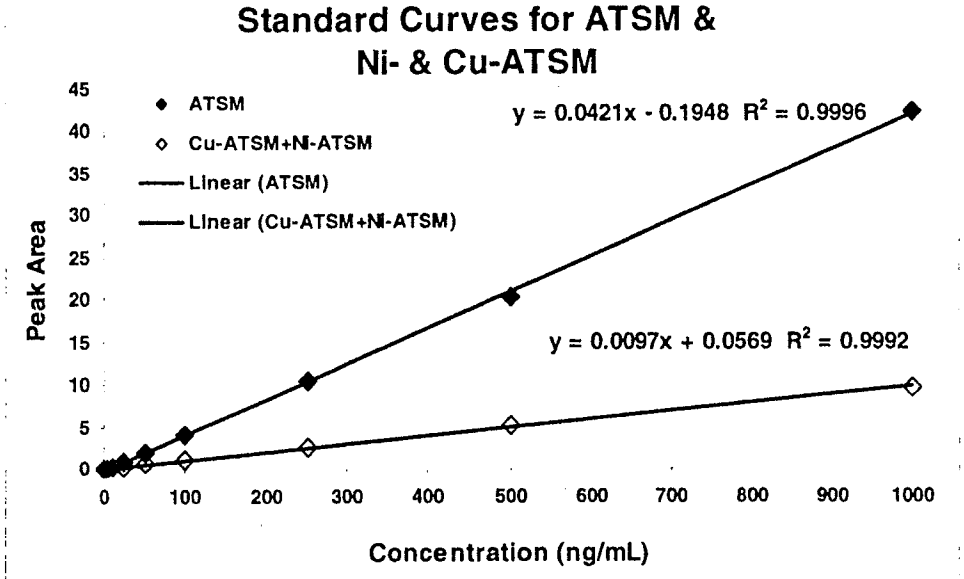


Table 1. Dose Formulation Samples for IITRI Project 2073-002-003

Group Number	Name on Vial Label	Preparation Date	Conc. (mg/mL)	Sampling Date	Sample # on Vial	ATSM Peak Area			ATSM Conc.	Ni+Cu-ATSM Peak Area			Ni+Cu-ATSM Conc.
						1	2	Mean	(ng/mL)	1	2	Mean	(ng/mL)
1	Vehicle (Concentration Sample)	5/14/2004	0	5/14/2004	2073002002-5/14/04-0-1a	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
1	Vehicle (Day8)	5/21/2004	0	5/21/2004	2073002002-5/21/04-0-1	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
1	Vehicle (Day14)	5/27/2004	0	5/27/2004	2073002002-5/27/04-0-1	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
2	CuATSM/H2ATSM (Top)	5/14/2004	0.015	5/14/2004	2073002002-5/14/04-0.015-1a	564.06	572.29	568.17	**13500.43**	89.06	91.40	90.23	**9296.13**
2	CuATSM/H2ATSM (Middle)	5/14/2004	0.015	5/14/2004	2073002002-5/14/04-0.015-1b	590.53	593.65	592.09	**14068.61**	92.87	92.94	92.91	**9572.01**
2	CuATSM/H2ATSM (Bottom)	5/14/2004	0.015	5/14/2004	2073002002-5/14/04-0.015-1c	602.04	578.71	590.37	**14027.70**	86.67	93.42	90.04	**9276.94**
2	CuATSM/H2ATSM (Day8)	5/21/2004	0.015	5/21/2004	2073002002-5/21/04-0.015-1	636.51	645.79	641.15	**15233.90**	79.79	80.44	80.11	**8253.32**
2	CuATSM/H2ATSM (Day14)	5/27/2004	0.015	5/27/2004	2073002002-5/27/04-0.015-1	799.85	804.93	802.39	**19063.70**	103.48	105.39	104.43	**10760.47**
3	CuATSM/H2ATSM (Top)	5/14/2004	0.030	5/14/2004	2073002002-5/14/04-0.030-1a	724.06	713.94	719.00	**17082.99**	170.22	176.14	173.18	**17847.87**
3	CuATSM/H2ATSM (Middle)	5/14/2004	0.030	5/14/2004	2073002002-5/14/04-0.030-1b	1108.90	1126.42	1117.66	**26552.44**	144.20	146.46	145.33	**14976.47**
3	CuATSM/H2ATSM (Bottom)	5/14/2004	0.030	5/14/2004	2073002002-5/14/04-0.030-1c	951.02	958.38	954.70	**22681.62**	111.27	113.14	112.20	**11561.61**
3	CuATSM/H2ATSM (Day8)	5/21/2004	0.030	5/21/2004	2073002002-5/21/04-0.030-1	1017.99	1020.28	1019.13	**24212.04**	147.16	149.73	148.45	**15297.85**
3	CuATSM/H2ATSM (Day14)	5/27/2004	0.030	5/27/2004	2073002002-5/27/04-0.030-1	1406.24	1406.53	1406.39	**33410.50**	232.64	234.80	233.72	**24088.97**

Table 2. Dose Formulation Samples for IITRI Project 2073-002-002

Group Number	Name on Vial Label	Preparation Date	Conc. (mg/mL)	Sampling Date	Sample # on Vial	ATSM Peak Area 1	ATSM Peak Area 2	ATSM Peak Area Mean	ATSM Conc. (ng/mL)	Ni+Cu-ATSM Peak Area 1	Ni+Cu-ATSM Peak Area 2	Ni+Cu-ATSM Peak Area Mean	Ni+Cu-ATSM Conc. (ng/mL)
1	Vehicle (Concentration Sample)	5/6/2004	0	5/6/2004	2073002002-5/6/04-0-1a	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
1	Vehicle (Day 8 Stability)	5/6/2004	0	5/13/2004	2073002002-5/6/04-0-2a	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
1	Vehicle (Day 14 Stability)	5/6/2004	0	5/19/2004	2073002002-5/6/04-0-3a	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
1	Vehicle (Day8)	5/13/2004	0	5/13/2004	2073002002-5/13/04-0-1a	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
1	Vehicle (Day14)	5/19/2004	0	5/19/2004	2073002002-5/19/04-0-1a	0.00	0.00	0.00	**0.00**	0.00	0.00	0.00	**0.00**
2	CuATSM/H2ATSM (Top)	5/6/2004	0.015	5/6/2004	2073002002-5/6/04-0.015-1a	513.23	499.91	506.57	**12037.23**	85.80	93.20	89.50	**9220.58**
2	CuATSM/H2ATSM (Middle)	5/6/2004	0.015	5/6/2004	2073002002-5/6/04-0.015-1b	663.49	655.93	659.71	**15674.60**	100.41	98.73	99.57	**10259.15**
2	CuATSM/H2ATSM (Bottom)	5/6/2004	0.015	5/6/2004	2073002002-5/6/04-0.015-1c	586.69	582.87	584.78	**13894.95**	108.23	110.12	109.17	**11249.15**
2	CuATSM/H2ATSM (Day 8 Stability)	5/6/2004	0.015	5/13/2004	2073002002-5/6/04-0.015-2a	274.84	273.64	274.24	**6518.58**	66.30	66.49	66.40	**6839.01**
2	CuATSM/H2ATSM (Day 14 Stability)	5/6/2004	0.015	5/19/2004	2073002002-5/6/04-0.015-3a	283.57	281.44	282.50	**6714.92**	81.12	82.91	82.01	**8449.27**
2	CuATSM/H2ATSM (Day8)	5/13/2004	0.015	5/13/2004	2073002002-5/13/04-0.015-1a	641.98	644.76	643.37	**15286.66**	79.71	81.56	80.64	**8307.14**
2	CuATSM/H2ATSM (Day14)	5/19/2004	0.015	5/19/2004	2073002002-5/19/04-0.015-1a	653.09	714.65	683.87	**16248.64**	83.13	73.23	78.18	**8054.12**
3	CuATSM/H2ATSM (Top)	5/6/2004	0.030	5/6/2004	2073002002-5/6/04-0.030-1a	1213.44	1211.34	1212.39	**28802.43**	167.65	169.27	168.46	**17360.82**
3	CuATSM/H2ATSM (Middle)	5/6/2004	0.030	5/6/2004	2073002002-5/6/04-0.030-1b	1153.25	1132.60	1142.93	**27152.54**	208.22	214.97	211.60	**21808.19**
3	CuATSM/H2ATSM (Bottom)	5/6/2004	0.030	5/6/2004	2073002002-5/6/04-0.030-1c	701.98	689.62	695.80	**16531.91**	211.85	215.61	213.73	**22027.89**
3	CuATSM/H2ATSM (Day 8 Stability)	5/6/2004	0.030	5/13/2004	2073002002-5/6/04-0.030-2a	197.60	194.16	195.88	**4657.31**	38.23	37.37	37.80	**3891.07**
3	CuATSM/H2ATSM (Day 14 Stability)	5/6/2004	0.030	5/19/2004	2073002002-5/6/04-0.030-3a	156.23	154.68	155.46	**3697.21**	49.71	51.08	50.39	**5189.12**
3	CuATSM/H2ATSM (Day8)	5/13/2004	0.030	5/13/2004	2073002002-5/13/04-0.030-1a	1621.32	1635.42	1628.37	**38683.26**	176.58	179.83	178.20	**18365.77**
3	CuATSM/H2ATSM (Day14)	5/19/2004	0.030	5/19/2004	2073002002-5/19/04-0.030-1a	1154.70	1146.17	1150.43	**27330.77**	223.47	226.46	224.97	**23186.50**

APPENDIX A

5
Note: The data contained in this report are confidential and the property of the U.S. Government. They are not to be disclosed to a third party, used in an IND or used in any other publications without the express written permission of the Development Therapeutics Program, DCTD, NCI.

HPLC Method for Determination of Cu-ATSM + H_2-ATSM

1. Reagents and Drugs

- Acetonitrile, HPLC grade (Fisher Chemicals A998-4)
- Methanol, HPLC grade (Fisher Chemicals A452-4)
- Cu-ATSM + H_2-ATSM (D729307-J/D1)

2. Preparation of standard stock solutions

Weigh 2.1 mg of Cu-ATSM + H_2-ATSM and dissolve in methanol in a polypropylene tube to make the final concentration of 1.0 mg/mL. Store at –80°C.

3. Preparation of mobile phase

The mobile phase is composed of 50:50 acetonitrile:ddH_2O (vol/vol). Prior to application, the mobile phase is filtered and degassed using Millipore glass filter system with nylon membrane (0.2 µm).

4. HPLC conditions

The HPLC system consists of a Hewlett Packard 1050 ChemStation with a UV detector (Agilent 1050 series). Determination of Cu-ATSM + H_2-ATSM is achieved using a Zorbax SB-18 (5 µm, 150×4.6 mm) analytical column with a LiChroCART 100 RP-18 guard column. The flow rate is 1 mL/min. The column elute is monitored by UV at 345 nm.

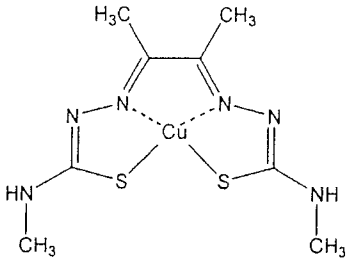
5. Preparation of standards

- Dilute Cu-ATSM + H_2-ATSM stock solution with methanol to prepare the serial standard concentrations of 0, 0.05, 0.10, 0.25, 0.5, 1.0, 2.5, 5.0 and 10.0µg/mL. (Daily freshly prepared standard solutions are required.)
- Mix 10 µL of standard solution with 90 µL of the mobile phase. This will yield standards with final Cu-ATSM + H_2-ATSM concentrations of 0, 0.005, 0.010, 0.025, 0.05, 0.1, 0.25, 0.5 and 1.0 µg/mL, respectively.

7. Quantification of Cu-ATSM and H_2-ATSM

Peak area is determined for quantification of Cu-ATSM and H_2-ATSM. Linear regression and correlation analysis is accomplished to establish the standard peak-area/concentration curves for Cu-ATSM + H_2-ATSM.

Cu-ATSM



Elemental Analysis;

	C	H	N	S
Expected; Calc for $CuC_8H_{14}S_2N_6$	29.85	4.38	26.11	19.92
Found (Cu JSL(1))	29.83	4.54	25.92	20.04
Found (Cu JSL(2))	29.54	4.50	25.66	20.00
Found (Cu JSL(3))	29.74	4.55	25.95	19.86

Mass Spectra;

LRFAB: Peak match to $[M + H]^+$ m/z = 321.9855

HRFAB: Peak match to $[M + H]^+$ m/z = 322.0095

ESI +ve: A 1 mg/ml solution of Cu-ATSM (M) was made up by dissolving 1 mg of material into 1 mL of ethanol. Of this freshly prepared solution 20 µL was removed and added to 200 µL of a 1:1 mixture of water and methanol. This was then directly infused at a flow rate of 10 µL/min into the water ZQ 4000 mass spectrometer. The conditions of the mass spectrometer were then adjusted to generate a signal of maximum intensity. Data was then collected using an ESI probe operating in the positive mode for a time frame of 2 minutes over the M/Z range of 150-600 Da. The major peak was observed at 321.88 Da which corresponds to $C_8H_{15}N_6S_2Cu$ or $[M + H]^+$. The isotopic distribution pattern around this peak matched exactly the theoretical pattern generated by Cu-ATSM.

GALBRAITH LABORATORIES, INC.

LABORATORY REPORT

Dr Jason Lewis
Washington Univ
School of Med CB8225
510 S Kingshwy Blvd
St Louis MO 63110

Report Date: 06/11/03

Purchase Order #: 68600P

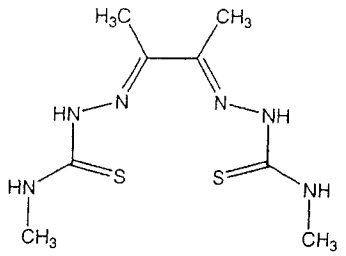
Fax Number: 314-362-9940

SAMPLE ID	LAB ID	ANALYSIS	RESULT(S)	
Cu JSL(1)	Q-4455	Sulfur	20.04	%
		Carbon	29.83	%
		Hydrogen	4.54	%
		Nitrogen	25.92	%
Cu JSL(2)	Q-4456	Sulfur	20.00	%
		Carbon	29.54	%
		Hydrogen	4.50	%
		Nitrogen	25.66	%
Cu JSL(3)	Q-4457	Sulfur	19.86	%
		Carbon	29.74	%
		Hydrogen	4.55	%
		Nitrogen	25.95	%

2323 Sycamore Drive
Knoxville, TN 37921-1700
TOLL FREE 877.449.8797

P.O. Box 51610
Knoxville, TN 37950-1610
FAX 865.546.7209

H_2ATSM



Elemental Analysis;

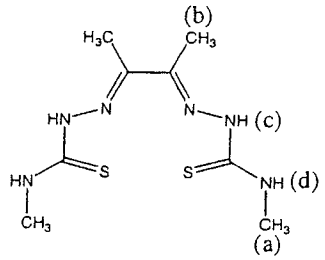
	C	H	N
Expected; Calc for $C_8H_{16}S_2N_6.¼H_2O$	36.40	6.30	31.83
Found (JSL 3697)	36.48	6.23	31.33
Found (JSL 3697 (b))	36.59	6.15	31.77

I have a large number of elemental analysis results, shown above are two representative samples. The results from an identical sample run twice do vary. This leads to the assumption that water is present. When calculated for different amounts of water present the elemental analysis result for all samples are consistent. The presence of water is confirmed by the NMR spectra (see below).

Mass Spectra;
HRFAB: Peak match to $[M + H]^+$ m/z = 261.0956

HREI: Molecular Ion Peak m/z = 260.0878

NMR δ(ppm), in DMSO-d_6;
The ^{1}H-NMR is somewhat difficult to interpret due to the tautomeric nature of the ligand.



2.203 (s, C<u>H</u>$_3$ (b), 6H); 3.011-3.026 (d, C<u>H</u>$_3$ (a), 6H); Doublet at 8.365 and singlet at 10.214 are not possible to assign due to tautomeric nature, however, they do correspond to the N<u>H</u> and intergrate for (C) and (d) as 4H consistent with the structure. Water is prensent in the NMR (confirming elemental analysis) at 3.338 ppm.

The ^{13}-NMR is very clean and consistent with structure. 11.657 (s, <u>C</u>H$_3$ (b)); 31.207 (s, <u>C</u>H$_3$ (a)); 147.977 (<u>C</u>=S); 178.471 (<u>C</u>=N).

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LABORATORY REPORT

Jason Lewis
Washington University
510 South Kingshighway Blvd
Campus Box 8225
St Louis MO 63110

Report Date: 03/24/97
Sample Received: 03/14/97
Purchase Order #: 60678R

SAMPLE ID	LAB ID	ANALYSIS	RESULTS	
JSL 3697	S-9796	Carbon	36.48	%
		Hydrogen	6.23	%
		Nitrogen	31.33	%

ICP:sc
D9

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LABORATORY REPORT

Jason Lewis
Washington University
510 South Kingshighway Blvd
Campus Box 8225
St Louis MO 63110

Report Date: 04/03/97
Sample Received: 03/25/97
Purchase Order #: 61782R

SAMPLE ID	LAB ID	ANALYSIS	RESULTS	
JSL 3697(b)	T-1071	Carbon	36.59	%
		Hydrogen	6.15	%
		Nitrogen	31.77	%

ICP:le
A8

Tennessee Quality Commitment Award 1996 BUILDING PARTNERSHIPS FOR CONTINUOUS IMPROVEMENT

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Other Carriers: 2323 Sycamore Drive · Knoxville, TN 37921-1750
Tel: (423) 546-1335 · Fax: (423) 546-7209

SIGMA-ALDRICH

Certificate of Analysis

Product Name	Dimethyl sulfoxide
Product Number	D1435
CAS Number	67-68-5
Molecular Formula	C_2H_6OS
Molecular Weight	78.13

TEST	SPECIFICATION	LOT 033K0640 RESULTS
IDENTITY	PASS	PASS
SPECIFIC GRAVITY	1.095 TO 1.101	1.099
CONGEALING TEMPERATURE	NLT 18.3 DEG C INDICATING NLT 99.9% C2H6OS	18.4 DEG C
REFRACTIVE INDEX	1.4755 TO 1.4775	1.4761
ACIDITY	PASS	PASS
WATER CONTENT BY KARL FISCHER	NMT 0.1%	0.017%
UV ABSORBANCE	PASS	PASS
SUBSTANCES DARKENED BY POTASSIUM HYDROXIDE	PASS	PASS
LIMIT OF DIMETHYL SULFONE	NMT 0.1%	PASS
LIMIT OF NONVOLATILE RESIDUE	PASS	PASS
		ALL RESULTS SUPPLIER DATA MEETS CURRENT USP REQUIRMENTS
SHELF LIFE SOP QC-12-006	2 YEARS	MARCH 2005
QC ACCEPTANCE DATE		MARCH 2003

Lori Schulz, Manager
Analytical Services

Baxter
Healthcare

MEDICATION DELIVERY
NORTH COVE FACILITY
Hwy 221 N PO Box 1390
Marion N.C. 28752
Telephone: (828) 756-4151
Fax: (828) 756-4821

Certificate of Analysis

Product: 0.9% Sodium Chloride, USP

Lot #: C604942

Code: 2B1323Q

Manufactured Date: 02/04/04

Expiry: 05/2005

TEST	LIMIT	RESULT
NaCl (g/L)	8.55 - 9.45 g/L	8.96 g/L
Sodium ID	Positive	Positive
Sodium ID- Flame	Positive	Positive
pH at 25 deg. C	4.5 - 7.0	5.6
Particle Analysis	NMT 25 ≥ 10 um	NMT 25
Particle Analysis	NMT 3 ≥ 25 um	NMT 3
Sterility	Pass Parametric Release	Pass
Endotoxin	Pass	Pass

This is to certify that this product was manufactured according to current GMP and fulfills the requirements of the Master Production Document.

M. LaRue 3-31-04
Prepared By / Date

Nancy P. Bartone 3-31-04
Verified By / Date

L. Lopez 3/31/04
Quality Management Approval

An ISO 9001: 2000
Certified Company
The Promise of Purity

pharmco™
PRODUCTS INC

CERTIFICATE OF ANALYSIS
ETHYL ALCOHOL 200 PROOF, ABSOLUTE
ACS/USP GRADE

LOT # PS5520
Q.C. # 0303124
Date / Date of Manufacture: 03/19/03
Current Catalog #: 111000200, 111USP200,
Old Cat#112000200, 112USP200, 111ACS200, or 112ACS200

TEST	SPECIFICATION	RESULT
Assay (ACS) (v/v)	NLT 99.5%	99.98%
Water (ACS) (v/v)	NMT 0.2%	0.07%
Proof @ 20C	NLT 199	199.9
Specific Gravity @ 20C	0.7900-0.7932	0.7906
Color (APHA) (ACS)	NMT 10	<10
Solubility in Water (ACS)	To Pass Test	Pass
Nonvolatile Residue (ACS)	NMT 0.001%	<0.001%
Nonvolatile Residue (USP)	NMT 0.0025%	<0.001%
Acetone/IPA (ACS, USP)	To Pass Tests	Pass
Titrable Acid (ACS)	NMT 0.0005 meq/g	Pass
Titrable Base (ACS)	NMT 0.0002 meq/g	Pass
Acidity (USP)	To Pass Test	Pass
Methanol (ACS)	NMT 0.1%	<0.1%
Methanol (USP)	To Pass Test	Pass
Substances Darkened by Sulfuric Acid (ACS)	To Pass Test	Pass
Substances Reducing Permanganate (ACS)	To Pass Test	Pass
ID Test A (USP)	To Pass Test	Pass
ID Test B (USP)	To Pass Test	Pass
Specific Gravity @ 15.56°C	NMT 0.7962	0.7937
Water Insoluble Substances	To Pass Test	Pass
Aldehydes and Other Foreign Organic Substances	To Pass Test	Pass
Amyl Alcohol/Nonvolatile, Carbonizable Substances	Not Detected	Pass
Ultraviolet Absorbance @ 240 nm (USP)	NMT 0.08	0.068
Ultraviolet Absorbance @ 270-340 nm (USP)	NMT 0.02	0.006
Ultra Violet Absorbance (ACS 9th ed.)	To Pass Test	Pass

Form: Ethanol, Pure, 200, ACS/USP, #101, Rev 2.3, 07/28/02

Approved by: R. Diaz, Technician

For Industrial, Pharmaceutical, Flavor & Fragrance or Lab Use. Not intended as an active substance in Food or Drug. Not to be considered a Medical Device. Not intended for use as a Disinfectant as defined by the EPA. The expiration date of this product is three years from the date of manufacture. (Rev. # disclaimer only: Rev 3.2 12/19/02 PD)

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Telephone: (203) 740-3471 Fax (203) 740-3483
E-Mail: paul@pharmco-prod.com
Website: www.pharmco-prod.com

SIGMA-ALDRICH

Certificate of Analysis

Product Name	Cyclophosphamide monohydrate
Product Number	21,870-7
Product Brand	ALDRICH
CAS Number	6055-19-2
Molecular Formula	$C_7H_{15}Cl_2N_2O_2P \cdot H_2O$
Molecular Weight	279.10

TEST	SPECIFICATION	LOT 11320MS RESULTS
APPEARANCE	WHITE CRYSTALLINE POWDER AND/OR CHUNKS	WHITE CRYSTALLINE POWDER
MELTING POINT		49.7-51.7 DEGREES CELSIUS
INFRARED SPECTRUM	CONFORMS TO STRUCTURE AND STANDARD AS ILLUSTRATED ON PAGE 920C OF EDITION I, VOLUME 1 OF 'THE ALDRICH LIBRARY OF FT-IR SPECTRA'.	CONFORMS TO STRUCTURE AND STANDARD AS ILLUSTRATED ON PAGE 1582D OF EDITION I, VOLUME 1 OF 'THE ALDRICH LIBRARY OF FT-IR SPECTRA'.
TITRATION	98.0% - 102.0% (WITH AGNO3 AFTER OXYGEN COMBUSTION)	98.3 % (WITH AGNO3 AFTER OXYGEN COMBUSTION)
TITRATION		6.93 % H2O (WITH 'KARL FISCHER' REAGENT)
SOLUBILITY		100MG/ML, H2O; CLEAR, COLORLESS SOLUTION
QUALITY CONTROL ACCEPTANCE DATE		NOVEMBER 1998

Ronnie J Martin, Supervisor
Quality Control

Appendix C: Individual Animal Data

Appendix C Table C-1

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 1-M SEX: MALE
DAY 1-DAY 29 DOSE: 0 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
801	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
802	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
803	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
804	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
805	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
806	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
807	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
808	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
809	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
810	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 1-M SEX: MALE
DAY 1-DAY 29 DOSE: 0 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
811	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	2	R7	DAY 14	DAY 16	2
	Eye Trauma Due To Bleed	4	R7	DAY 22	DAY 28	2
	Normal			DAY 1	DAY 8	2
812	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	2	R7	DAY 16	DAY 16	1
	Normal			DAY 1	DAY 28	5
813	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
814	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
815	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 2-M SEX: MALE
DAY 1-DAY 29 DOSE: 0.075 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
831	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
832	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
833	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
834	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
835	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
836	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
837	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
838	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
839	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
840	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 2-M SEX: MALE
DAY 1-DAY 29 DOSE: 0.075 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
841	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
842	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	2	R7	DAY 22	DAY 28	2
	Normal			DAY 1	DAY 16	4
843	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
844	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
845	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 3-M SEX: MALE
DAY 1-DAY 29 DOSE: 0.150 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
861	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
862	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
863	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
864	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
865	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
866	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
867	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
868	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
869	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
870	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 3-M SEX: MALE
DAY 1-DAY 29 DOSE: 0.150 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
871	Recovery Sacrifice			DAY 29	DAY 29	1
	Lesion - ulcerated	2	M1	DAY 28	DAY 28	1
	Eye Trauma Due To Bleed	3	R7	DAY 14	DAY 28	4
	Normal			DAY 1	DAY 8	2
872	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
873	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
874	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
875	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 1-F SEX: FEMALE
DAY 1-DAY 29 DOSE: 0 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
816	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
817	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
818	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
819	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
820	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
821	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
822	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
823	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
824	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
825	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 1-F SEX: FEMALE
DAY 1-DAY 29 DOSE: 0 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
826	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	1	R7	DAY 22	DAY 28	2
	Normal			DAY 1	DAY 16	4
827	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	1	R7	DAY 16	DAY 28	3
	Normal			DAY 1	DAY 14	3
828	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
829	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
830	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 2-F SEX: FEMALE
DAY 1-DAY 29 DOSE: 0.075 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
846	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
847	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
848	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
849	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
850	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
851	Eye Trauma Due To Bleed	1	R7	DAY 14	DAY 14	1
	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 8	2
852	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
853	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
854	Eye Trauma Due To Bleed	3	R7	DAY 14	DAY 14	1
	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 8	2
855	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 2-F SEX: FEMALE
DAY 1-DAY 29 DOSE: 0.075 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
856	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	2	R7	DAY 16	DAY 16	1
	Eye Trauma Due To Bleed	4	R7	DAY 22	DAY 28	2
	Normal			DAY 1	DAY 14	3
857	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
858	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
859	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
860	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 3-F SEX: FEMALE
DAY 1-DAY 29 DOSE: 0.150 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
876	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
877	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
878	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
879	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
880	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
881	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
882	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
883	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
884	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3
885	Terminal Sacrifice			DAY 15	DAY 15	1
	Normal			DAY 1	DAY 14	3

Appendix C Table C-1 (cont.)

INDIVIDUAL CLINICAL SIGNS

STUDY: 2073002 GROUP: 3-F SEX: FEMALE
DAY 1-DAY 29 DOSE: 0.150 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
886	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
887	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	4	R7	DAY 14	DAY 28	4
	Normal			DAY 1	DAY 8	2
888	Recovery Sacrifice			DAY 29	DAY 29	1
	Eye Trauma Due To Bleed	1	R7	DAY 22	DAY 28	2
	Normal			DAY 1	DAY 16	4
889	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6
890	Recovery Sacrifice			DAY 29	DAY 29	1
	Normal			DAY 1	DAY 28	6

Appendix C Table C-2

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 1-M SEX: MALE (TREATMENT PERIOD)
DOSE: 0 (mg/kg)

ANIMAL #	DAY 1	DAY 5	DAY 8	DAY 12	DAY 14
801	221	231	243	247	257
802	199	210	217	227	232
803	213	223	229	238	241
804	203	215	225	230	237
805	207	216	225	235	243
806	209	223	233	238	241
807	203	218	229	234	241
808	197	206	217	225	228
809	208	223	231	239	244
810	210	221	230	237	243
811	204	210	217	225	234
812	201	211	221	229	234
813	212	225	235	241	248
814	208	218	228	234	240
815	199	210	221	223	229
MEAN	206	217	227	233	239
S.D.	6.4	7.0	7.4	6.8	7.5
N	15	15	15	15	15

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 2-M SEX: MALE (TREATMENT PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 1	DAY 5	DAY 8	DAY 12	DAY 14
831	198	210	215	219	225
832	201	209	215	223	228
833	209	215	225	235	239
834	209	221	230	236	242
835	222	233	244	254	259
836	214	224	235	246	254
837	204	206	217	226	231
838	208	216	229	233	238
839	200	209	220	225	231
840	205	209	219	228	233
841	209	220	231	235	240
842	208	221	228	235	243
843	197	204	215	221	230
844	207	213	224	233	241
845	212	218	234	243	251
MEAN	207	215	225	233	239
S.D.	6.5	7.8	8.7	9.7	9.9
N	15	15	15	15	15

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 3-M SEX: MALE (TREATMENT PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 1	DAY 5	DAY 8	DAY 12	DAY 14
861	207	223	236	246	254
862	209	226	234	244	249
863	211	219	227	237	242
864	222	238	247	253	261
865	203	211	221	228	232
866	204	213	223	231	239
867	199	210	217	229	235
868	199	208	218	222	227
869	203	212	218	230	235
870	207	218	226	230	234
871	211	217	228	227	236
872	208	216	224	233	239
873	212	218	225	230	236
874	211	218	226	231	238
875	210	218	228	235	241
MEAN	208	218	227	234	240
S.D.	5.8	7.4	7.8	8.2	8.8
N	15	15	15	15	15

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 1-F SEX: FEMALE (TREATMENT PERIOD)
DOSE: 0 (mg/kg)

ANIMAL #	DAY 1	DAY 5	DAY 8	DAY 12	DAY 14
816	132	140	145	150	154
817	140	146	151	154	159
818	145	149	153	158	157
819	150	153	161	162	166
820	143	149	157	158	162
821	143	147	151	153	154
822	146	149	157	157	159
823	136	140	147	151	153
824	147	149	156	156	160
825	136	142	147	146	152
826	145	150	159	155	159
827	144	149	159	159	160
828	149	153	159	162	166
829	143	148	155	152	157
830	139	143	152	150	155
MEAN	143	147	154	155	158
S.D.	5.1	4.2	5.0	4.6	4.3
N	15	15	15	15	15

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 2-F SEX: FEMALE (TREATMENT PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 1	DAY 5	DAY 8	DAY 12	DAY 14
846	144	147	151	149	151
847	145	149	155	154	159
848	145	148	153	151	155
849	138	143	147	147	153
850	144	146	146	151	155
851	143	150	159	160	166
852	140	147	152	149	155
853	140	143	149	150	152
854	143	148	155	152	158
855	138	141	146	146	152
856	143	149	155	156	157
857	136	138	142	143	147
858	148	149	153	155	157
859	149	152	161	162	165
860	151	157	163	163	165
MEAN	143	147	152	153	156
S.D.	4.2	4.6	5.9	5.8	5.5
N	15	15	15	15	15

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 3-F SEX: FEMALE (TREATMENT PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 1	DAY 5	DAY 8	DAY 12	DAY 14
876	143	150	152	155	157
877	140	145	153	157	158
878	149	155	155	158	163
879	144	148	152	152	158
880	148	151	158	161	164
881	147	151	159	158	162
882	145	148	151	153	154
883	142	148	152	152	157
884	137	140	146	146	151
885	140	145	150	147	153
886	140	142	147	142	148
887	140	149	154	146	153
888	142	147	153	154	159
889	142	146	149	148	151
890	151	155	161	160	165
MEAN	143	148	153	153	157
S.D.	4.0	4.2	4.2	5.8	5.2
N	15	15	15	15	15

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 1-M SEX: MALE (RECOVERY PERIOD)
DOSE: 0 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28
801	e	e	e	e	e
802	e	e	e	e	e
803	e	e	e	e	e
804	e	e	e	e	e
805	e	e	e	e	e
806	e	e	e	e	e
807	e	e	e	e	e
808	e	e	e	e	e
809	e	e	e	e	e
810	e	e	e	e	e
811	234	251	235	251	262
812	233	246	255	266	275
813	247	259	269	283	292
814	244	246	253	263	270
815	230	242	245	258	267
MEAN	238	249	251	264	273
S.D.	7.4	6.5	12.6	11.9	11.5
N	5	5	5	5	5

e: Terminal Sacrifice

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 2-M SEX: MALE (RECOVERY PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28
831	e	e	e	e	e
832	e	e	e	e	e
833	e	e	e	e	e
834	e	e	e	e	e
835	e	e	e	e	e
836	e	e	e	e	e
837	e	e	e	e	e
838	e	e	e	e	e
839	e	e	e	e	e
840	e	e	e	e	e
841	244	253	256	270	276
842	241	255	260	274	283
843	231	243	252	265	273
844	244	257	263	275	282
845	254	267	274	283	290
MEAN	243	255	261	273	281
S.D.	8.2	8.6	8.4	6.7	6.6
N	5	5	5	5	5

e: Terminal Sacrifice

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 3-M SEX: MALE (RECOVERY PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28
861	e	e	e	e	e
862	e	e	e	e	e
863	e	e	e	e	e
864	e	e	e	e	e
865	e	e	e	e	e
866	e	e	e	e	e
867	e	e	e	e	e
868	e	e	e	e	e
869	e	e	e	e	e
870	e	e	e	e	e
871	237	228	230	251	261
872	240	252	261	275	281
873	235	245	252	266	272
874	239	248	258	270	275
875	244	252	257	270	273
MEAN	239	245	252	266	272
S.D.	3.4	9.9	12.5	9.2	7.3
N	5	5	5	5	5

e: Terminal Sacrifice

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 1-F DOSE: 0 (mg/kg) SEX: FEMALE (RECOVERY PERIOD)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28
816	e	e	e	e	e
817	e	e	e	e	e
818	e	e	e	e	e
819	e	e	e	e	e
820	e	e	e	e	e
821	e	e	e	e	e
822	e	e	e	e	e
823	e	e	e	e	e
824	e	e	e	e	e
825	e	e	e	e	e
826	159	165	167	170	169
827	159	162	164	165	167
828	164	176	179	183	188
829	156	162	163	168	172
830	156	159	161	167	171
MEAN	159	165	167	171	173
S.D.	3.3	6.6	7.2	7.2	8.4
N	5	5	5	5	5

e: Terminal Sacrifice

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 2-F SEX: FEMALE (RECOVERY PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28
846	e	e	e	e	e
847	e	e	e	e	e
848	e	e	e	e	e
849	e	e	e	e	e
850	e	e	e	e	e
851	e	e	e	e	e
852	e	e	e	e	e
853	e	e	e	e	e
854	e	e	e	e	e
855	e	e	e	e	e
856	162	158	160	167	171
857	149	153	156	159	160
858	156	160	163	169	171
859	165	174	174	179	183
860	166	175	177	180	182
MEAN	160	164	166	171	173
S.D.	7.1	9.9	9.1	8.8	9.4
N	5	5	5	5	5

e: Terminal Sacrifice

Appendix C Table C-2 (cont.)

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 2073002 GROUP: 3-F SEX: FEMALE (RECOVERY PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28
876	e	e	e	e	e
877	e	e	e	e	e
878	e	e	e	e	e
879	e	e	e	e	e
880	e	e	e	e	e
881	e	e	e	e	e
882	e	e	e	e	e
883	e	e	e	e	e
884	e	e	e	e	e
885	e	e	e	e	e
886	148	147	148	156	159
887	151	159	159	168	172
888	159	164	167	172	177
889	151	157	159	163	169
890	165	169	172	177	181
MEAN	155	159	161	167	172
S.D.	7.0	8.3	9.1	8.1	8.4
N	5	5	5	5	5

e: Terminal Sacrifice

Appendix C Table C-3

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 1-M SEX: MALE (TREATMENT PERIOD)
DOSE: 0 (mg/kg)

ANIMAL #	DAY 5	DAY 8	DAY 12	DAY 14	TOTAL GAIN
801	10	12	4	10	36
802	11	7	10	5	33
803	10	6	9	3	28
804	12	10	5	7	34
805	9	9	10	8	36
806	14	10	5	3	32
807	15	11	5	7	38
808	9	11	8	3	31
809	15	8	8	5	36
810	11	9	7	6	33
811	6	7	8	9	30
812	10	10	8	5	33
813	13	10	6	7	36
814	10	10	6	6	32
815	11	11	2	6	30
MEAN	11	9	7	6	33
S.D.	2.4	1.7	2.3	2.1	2.8
N	15	15	15	15	15

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 2-M SEX: MALE (TREATMENT PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 5	DAY 8	DAY 12	DAY 14	TOTAL GAIN
831	12	5	4	6	27
832	8	6	8	5	27
833	6	10	10	4	30
834	12	9	6	6	33
835	11	11	10	5	37
836	10	11	11	8	40
837	2	11	9	5	27
838	8	13	4	5	30
839	9	11	5	6	31
840	4	10	9	5	28
841	11	11	4	5	31
842	13	7	7	8	35
843	7	11	6	9	33
844	6	11	9	8	34
845	6	16	9	8	39
MEAN	8	10	7	6	32
S.D.	3.2	2.7	2.4	1.6	4.3
N	15	15	15	15	15

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 3-M SEX: MALE (TREATMENT PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 5	DAY 8	DAY 12	DAY 14	TOTAL GAIN
861	16	13	10	8	47
862	17	8	10	5	40
863	8	8	10	5	31
864	16	9	6	8	39
865	8	10	7	4	29
866	9	10	8	8	35
867	11	7	12	6	36
868	9	10	4	5	28
869	9	6	12	5	32
870	11	8	4	4	27
871	6	11	-1	9	25
872	8	8	9	6	31
873	6	7	5	6	24
874	7	8	5	7	27
875	8	10	7	6	31
MEAN	10	9	7	6	32
S.D.	3.6	1.8	3.5	1.6	6.3
N	15	15	15	15	15

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 1-F DOSE: 0 (mg/kg) SEX: FEMALE (TREATMENT PERIOD)

ANIMAL #	DAY 5	DAY 8	DAY 12	DAY 14	TOTAL GAIN
816	8	5	5	4	22
817	6	5	3	5	19
818	4	4	5	-1	12
819	3	8	1	4	16
820	6	8	1	4	19
821	4	4	2	1	11
822	3	8	0	2	13
823	4	7	4	2	17
824	2	7	0	4	13
825	6	5	-1	6	16
826	5	9	-4	4	14
827	5	10	0	1	16
828	4	6	3	4	17
829	5	7	-3	5	14
830	4	9	-2	5	16
MEAN	5	7	1	3	16
S.D.	1.5	1.9	2.8	1.9	2.9
N	15	15	15	15	15

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 2-F SEX: FEMALE (TREATMENT PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 5	DAY 8	DAY 12	DAY 14	TOTAL GAIN
846	3	4	-2	2	7
847	4	6	-1	5	14
848	3	5	-2	4	10
849	5	4	0	6	15
850	2	0	5	4	11
851	7	9	1	6	23
852	7	5	-3	6	15
853	3	6	1	2	12
854	5	7	-3	6	15
855	3	5	0	6	14
856	6	6	1	1	14
857	2	4	1	4	11
858	1	4	2	2	9
859	3	9	1	3	16
860	6	6	0	2	14
MEAN	4	5	0	4	13
S.D.	1.9	2.2	2.1	1.8	3.7
N	15	15	15	15	15

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 3-F SEX: FEMALE (TREATMENT PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 5	DAY 8	DAY 12	DAY 14	TOTAL GAIN
876	7	2	3	2	14
877	5	8	4	1	18
878	6	0	3	5	14
879	4	4	0	6	14
880	3	7	3	3	16
881	4	8	-1	4	15
882	3	3	2	1	9
883	6	4	0	5	15
884	3	6	0	5	14
885	5	5	-3	6	13
886	2	5	-5	6	8
887	9	5	-8	7	13
888	5	6	1	5	17
889	4	3	-1	3	9
890	4	6	-1	5	14
MEAN	5	5	0	4	14
S.D.	1.8	2.2	3.3	1.9	2.9
N	15	15	15	15	15

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 1-M SEX: MALE (RECOVERY PERIOD)
DOSE: 0 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28	TOTAL@ GAIN
801	e	e	e	e	e	--
802	e	e	e	e	e	--
803	e	e	e	e	e	--
804	e	e	e	e	e	--
805	e	e	e	e	e	--
806	e	e	e	e	e	--
807	e	e	e	e	e	--
808	e	e	e	e	e	--
809	e	e	e	e	e	--
810	e	e	e	e	e	--
811	0	17	-16	16	11	28
812	-1	13	9	11	9	41
813	-1	12	10	14	9	44
814	4	2	7	10	7	30
815	1	12	3	13	9	38
MEAN	1	11	3	13	9	36
S.D.	2.1	5.5	10.7	2.4	1.4	6.9
N	5	5	5	5	5	5

@: Total Gain for Days 15-28
--: Data Unavailable e: Terminal Sacrifice

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 2-M SEX: MALE (RECOVERY PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28	TOTAL@ GAIN
831	e	e	e	e	e	--
832	e	e	e	e	e	--
833	e	e	e	e	e	--
834	e	e	e	e	e	--
835	e	e	e	e	e	--
836	e	e	e	e	e	--
837	e	e	e	e	e	--
838	e	e	e	e	e	--
839	e	e	e	e	e	--
840	e	e	e	e	e	--
841	4	9	3	14	6	36
842	-2	14	5	14	9	40
843	1	12	9	13	8	43
844	3	13	6	12	7	41
845	3	13	7	9	7	39
MEAN	2	12	6	12	7	40
S.D.	2.4	1.9	2.2	2.1	1.1	2.6
N	5	5	5	5	5	5

@: Total Gain for Days 15-28
--: Data Unavailable e: Terminal Sacrifice

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 3-M SEX: MALE (RECOVERY PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28	TOTAL@ GAIN
861	e	e	e	e	e	--
862	e	e	e	e	e	--
863	e	e	e	e	e	--
864	e	e	e	e	e	--
865	e	e	e	e	e	--
866	e	e	e	e	e	--
867	e	e	e	e	e	--
868	e	e	e	e	e	--
869	e	e	e	e	e	--
870	e	e	e	e	e	--
871	1	-9	2	21	10	25
872	1	12	9	14	6	42
873	-1	10	7	14	6	36
874	1	9	10	12	5	37
875	3	8	5	13	3	32
MEAN	1	6	7	15	6	34
S.D.	1.4	8.5	3.2	3.6	2.5	6.3
N	5	5	5	5	5	5

@: Total Gain for Days 15-28
--: Data Unavailable e: Terminal Sacrifice

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 1-F DOSE: 0 (mg/kg) SEX: FEMALE (RECOVERY PERIOD)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28	TOTAL@ GAIN
816	e	e	e	e	e	--
817	e	e	e	e	e	--
818	e	e	e	e	e	--
819	e	e	e	e	e	--
820	e	e	e	e	e	--
821	e	e	e	e	e	--
822	e	e	e	e	e	--
823	e	e	e	e	e	--
824	e	e	e	e	e	--
825	e	e	e	e	e	--
826	0	6	2	3	-1	10
827	-1	3	2	1	2	7
828	-2	12	3	4	5	22
829	-1	6	1	5	4	15
830	1	3	2	6	4	16
MEAN	-1	6	2	4	3	14
S.D.	1.1	3.7	0.7	1.9	2.4	5.8
N	5	5	5	5	5	5

@: Total Gain for Days 15-28
--: Data Unavailable e: Terminal Sacrifice

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 2-F SEX: FEMALE (RECOVERY PERIOD)
DOSE: 0.075 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28	TOTAL@ GAIN
846	e	e	e	e	e	--
847	e	e	e	e	e	--
848	e	e	e	e	e	--
849	e	e	e	e	e	--
850	e	e	e	e	e	--
851	e	e	e	e	e	--
852	e	e	e	e	e	--
853	e	e	e	e	e	--
854	e	e	e	e	e	--
855	e	e	e	e	e	--
856	5	-4	2	7	4	14
857	2	4	3	3	1	13
858	-1	4	3	6	2	14
859	0	9	0	5	4	18
860	1	9	2	3	2	17
MEAN	1	4	2	5	3	15
S.D.	2.3	5.3	1.2	1.8	1.3	2.2
N	5	5	5	5	5	5

@: Total Gain for Days 15-28
--: Data Unavailable e: Terminal Sacrifice

Appendix C Table C-3 (cont.)

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 2073002 GROUP: 3-F SEX: FEMALE (RECOVERY PERIOD)
DOSE: 0.150 (mg/kg)

ANIMAL #	DAY 15	DAY 19	DAY 22	DAY 26	DAY 28	TOTAL@ GAIN
876	e	e	e	e	e	--
877	e	e	e	e	e	--
878	e	e	e	e	e	--
879	e	e	e	e	e	--
880	e	e	e	e	e	--
881	e	e	e	e	e	--
882	e	e	e	e	e	--
883	e	e	e	e	e	--
884	e	e	e	e	e	--
885	e	e	e	e	e	--
886	0	-1	1	8	3	11
887	-2	8	0	9	4	19
888	0	5	3	5	5	18
889	0	6	2	4	6	18
890	0	4	3	5	4	16
MEAN	0	4	2	6	4	16
S.D.	0.9	3.4	1.3	2.2	1.1	3.2
N	5	5	5	5	5	5

@: Total Gain for Days 15-28
--: Data Unavailable e: Terminal Sacrifice

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4

Individual Animal Functional Observational Battery Tests

Foot Splay Data [a]

Group 1: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM)

Animal Number	Sex	Study Day -1 (Pre-Study) (cm)	Study Day 14 (cm)	Study Day 28 (cm)
806	M	4.0	5.0	-- [b]
807	M	4.0	6.6	--
808	M	5.8	5.4	--
809	M	5.5	6.8	--
810	M	4.4	5.6	--
811	M	5.1	6.0	5.4
812	M	3.6	6.4	5.1
813	M	3.6	6.5	6.3
814	M	4.5	6.5	5.2
815	M	4.2	5.8	6.0
821	F	4.4	4.2	--
822	F	3.9	4.5	--
823	F	3.4	4.8	--
824	F	3.5	4.4	--
825	F	3.3	4.6	--
826	F	3.2	3.8	3.6
827	F	4.0	4.0	4.4
828	F	4.6	2.9	4.0
829	F	3.1	5.5	4.3
830	F	3.6	4.4	4.8

[a] Average of 2 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Foot Splay Data [a]

Group 2: 0.075 mg/kg/day CuATSM/H_2ATSM

Animal Number	Sex	Study Day -1 (Pre-Study) (cm)	Study Day 14 (cm)	Study Day 28 (cm)
836	M	5.3	5.7	-- [b]
837	M	4.8	6.2	--
838	M	4.1	5.1	--
839	M	4.3	5.9	--
840	M	4.6	5.5	--
841	M	5.7	7.5	6.9
842	M	3.9	5.6	5.1
843	M	4.2	5.8	6.3
844	M	3.9	6.8	7.2
845	M	5.8	6.5	6.1
851	F	3.9	4.6	--
852	F	3.6	4.0	--
853	F	2.4	4.3	--
854	F	3.7	5.8	--
855	F	3.2	4.9	--
856	F	4.4	3.7	2.8
857	F	4.1	4.5	4.3
858	F	3.2	4.2	4.7
859	F	5.7	5.8	5.7
860	F	4.0	4.0	4.9

[a] Average of 2 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Foot Splay Data [a]

Group 3: 0.150 mg/kg/day CuATSM/H_2ATSM

Animal Number	Sex	Study Day -1 (Pre-Study) (cm)	Study Day 14 (cm)	Study Day 28 (cm)
866	M	4.5	5.8	-- [b]
867	M	5.0	6.1	--
868	M	4.3	6.1	--
869	M	4.5	5.5	--
870	M	3.8	5.9	--
871	M	4.1	5.2	4.0
872	M	5.1	5.0	4.4
873	M	4.2	4.0	3.0
874	M	4.5	6.2	6.1
875	M	4.5	4.8	4.8
881	F	3.5	4.0	--
882	F	5.4	5.6	--
883	F	3.9	4.0	--
884	F	4.6	4.5	--
885	F	4.9	6.2	--
886	F	3.9	4.4	4.0
887	F	4.3	4.0	3.9
888	F	5.0	3.3	4.9
889	F	2.9	3.0	2.7
890	F	4.3	4.6	4.9

[a] Average of 2 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Forelimb Grip Strength Data [a]

Group 1: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM)

Animal Number	Sex	Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
806	M	700	950	-- [b]
807	M	692	800	--
808	M	658	767	--
809	M	700	708	--
810	M	717	625	--
811	M	642	892	658
812	M	692	850	867
813	M	492	800	767
814	M	625	783	767
815	M	683	742	708
821	F	517	592	--
822	F	583	592	--
823	F	592	525	--
824	F	617	433	--
825	F	500	400	--
826	F	542	392	383
827	F	600	550	525
828	F	592	517	533
829	F	533	475	517
830	F	608	733	717

[a] Average of 3 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Forelimb Grip Strength Data [a]

Group 2: 0.075 mg/kg/day CuATSM/H_2ATSM

Animal Number	Sex	Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
836	M	700	850	-- [b]
837	M	675	808	--
838	M	867	750	--
839	M	683	833	--
840	M	692	867	--
841	M	750	933	792
842	M	767	783	708
843	M	767	850	775
844	M	675	775	608
845	M	692	892	783
851	F	550	525	--
852	F	617	375	--
853	F	550	617	--
854	F	592	625	--
855	F	550	650	--
856	F	483	508	617
857	F	600	675	492
858	F	625	692	517
859	F	617	658	750
860	F	575	683	567

[a] Average of 3 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Forelimb Grip Strength Data [a]

Group 3: 0.150 mg/kg/day CuATSM/H_2ATSM

Animal Number	Sex	Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
866	M	758	850	-- [b]
867	M	625	867	--
868	M	675	867	--
869	M	717	725	--
870	M	775	867	--
871	M	667	800	900
872	M	667	633	692
873	M	717	742	592
874	M	708	925	800
875	M	700	642	708
881	F	575	708	--
882	F	642	600	--
883	F	683	667	--
884	F	542	608	--
885	F	508	692	--
886	F	675	625	583
887	F	550	492	450
888	F	633	642	650
889	F	533	675	467
890	F	508	508	642

[a] Average of 3 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Hindlimb Grip Strength Data [a]

Group 1: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM)

Animal Number	Sex	Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
806	M	500	675	-- [b]
807	M	675	933	--
808	M	575	733	--
809	M	817	592	--
810	M	733	883	--
811	M	550	1050	600
812	M	708	967	800
813	M	658	667	733
814	M	492	925	708
815	M	733	750	700
821	F	625	500	--
822	F	717	675	--
823	F	575	583	--
824	F	575	450	--
825	F	592	333	--
826	F	433	542	375
827	F	550	508	592
828	F	475	500	417
829	F	433	383	417
830	F	658	492	675

[a] Average of 3 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Hindlimb Grip Strength Data [a]

Group 2: 0.075 mg/kg/day CuATSM/H_2ATSM

Animal Number	Sex	Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
836	M	808	792	-- [b]
837	M	650	600	--
838	M	800	575	--
839	M	608	667	--
840	M	567	933	--
841	M	900	717	608
842	M	900	742	642
843	M	917	592	592
844	M	667	500	708
845	M	642	692	842
851	F	608	433	--
852	F	483	433	--
853	F	608	625	--
854	F	833	408	--
855	F	492	592	--
856	F	433	367	325
857	F	417	500	600
858	F	667	392	375
859	F	683	650	642
860	F	450	733	567

[a] Average of 3 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-4 (cont.)

Individual Animal Functional Observational Battery Tests

Hindlimb Grip Strength Data [a]

Group 3: 0.150 mg/kg/day CuATSM/H_2ATSM

Animal Number	Sex	Study Day -1 (Pre-Study) (g)	Study Day 14 (g)	Study Day 28 (g)
866	M	767	633	-- [b]
867	M	650	1075	--
868	M	783	842	--
869	M	767	1050	--
870	M	700	1067	--
871	M	950	1075	783
872	M	583	775	467
873	M	717	592	392
874	M	700	833	633
875	M	650	617	517
881	F	533	900	--
882	F	775	858	--
883	F	583	792	--
884	F	550	467	--
885	F	650	525	--
886	F	800	483	650
887	F	683	617	517
888	F	750	908	600
889	F	517	483	525
890	F	500	592	525

[a] Average of 3 values
[b] --, Data unavailable; animal was sacrificed on Study Day 15

Appendix C Table C-5

Functional Observational Battery Key

I. HOME CAGE OBSERVATIONS

Posture:
1. asleep, lying on side, or curled up
2. lying on side, resting but awake
3. sitting or standing normally
4. rearing
5. hunched over

Palpebral Closure:
1. eyelids wide open
2. eyelids slightly drooping
3. ptosis; drooping eyelids (half closed)
4. eyelids completely shut

Convulsions or tremor:
1. present
   a) clonic (contraction followed by relaxation)
   b) tonic (constant contraction and extension of hindlimb muscles)
2. absent

Biting:
1. none
2. cage biting
3. self-destructive

Vocalizations:
1. absent
2. present

Reflexes (click response inside the cage):
1. no reaction
2. slight reaction, ear flick or evidence that snap was heard
3. more energetic response than 2, may include vocalization
4. freezes, actual muscle contractions
5. bizarre reaction (jumps, bites, or attacks)

II. OBSERVATIONS MADE WHILE HANDLING THE ANIMAL

Ease of Removal from Cage:
1. easy, little or no vocalization, handled without resistance
2. moderately difficult, rat rears, often following investigators hand
3. difficult; runs around cage; is hard to grab, with and without vocalization

Ease of Handling Rat in Hand (and throughout remainder of observations):
1. moderately easy, vocalization, handled without resistance
2. easy, but alert, limbs may be pulled against body
3. difficult, squirming, twisting, attempting to bite with or without vocalization

Lacrimation:
1. none
2. slight
3. severe

Salivation:
1. none
2. slight
3. severe

Fur Appearance:
1. normal
2. slightly soiled
3. very soiled, crusty
4. rough
5. pilo erection

Appendix C Table C-5 (cont.)

Functional Observational Battery Key

Gait Description:
1. normal
2. impairment
   a) uncoordinated movement (*i.e.*, ataxia)
   b) walking on toes
   c) splayed hindlimbs
   d) exaggerated hindlimb flexion
   e) staggered gait
   f) dragging hindlimbs
   g) unable to walk
   h) other (*e.g.*, rolling over, sleeping, convulsions)

Diarrhea:
1. absent
2. present
   a) slight
   b) moderate
   c) severe

Urine:
a. none
b. few (number of spots in parenthesis, if counted)
c. abundant

Tail Pinch (metal tweezers are used to squeeze the tail approximately 5 cm distal to the body):
1. no reaction
2. turns and walks away, may include vocalization
3. turns quickly and walks away, may include vocalization
4. freezes, actual muscle contraction
5. bizarre reaction, jumps, bites, or attacks

Pupil Response (beam from light is brought in from the side the rat's head and changes in direction is noted):
1. pupil response present
2. pupil response absent

Eye Blink Response (corner of eye is touched gently with a cotton thread):
1. eye blink response present
2. eye blink response absent

Vision (is checked by introducing a visual stimulus from a blind spot on the right or left side of the rat, or from above the rat's head):
1. Positive response: a) freezing b) orient head in the direction of the stimulus
2. No response

Hindlimb Extension (animal is placed on table top and lifted and presence or absence of normal hindlimb extension is noted):
1. hindlimb extension present
2. hindlimb extension absent

Catalepsy:
1. Present
2. Absent

Righting Reflex:
+ = Positive
– = Negative

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6

Individual Animal Functional Observational Battery Observations

Group 1 Males: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day -1 (Pre-Study)

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
806	2	1	2	1	1	2	1	1	34.5	1	1
807	2	1	2	1	1	2	1	1	34.6	1	1
808	2	1	2	1	1	2	1	1	33.8	1	1
809	2	1	2	1	1	2	1	1	34.7	1	1
810	2	1	2	1	1	1	1	1	34.5	1	1
811	2	1	2	1	1	2	1	1	35.6	1	1
812	2	1	2	1	1	2	1	1	35.1	1	1
813	2	1	2	1	1	2	1	1	34.7	1	1
814	2	1	2	1	1	2	1	1	35.2	1	1
815	2	1	2	1	1	1	1	1	35.9	1	1

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Males: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day -1 (Pre-Study)

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g) [a]
806	1	1	1	a	2	1	1	1a	1	2	+	204
807	1	1	1	a	2	1	1	1b	1	2	+	197
808	1	1	1	a	2	1	1	1b	1	2	+	191
809	1	1	1	a	2	1	1	1a	1	2	+	200
810	1	1	1	a	2	1	1	1a	1	2	+	203
811	1	1	1	a	2	1	1	1b	1	2	+	201
812	1	1	1	a	2	1	1	1b	1	2	+	195
813	1	1	1	a	2	1	1	1b	1	2	+	206
814	1	1	1	a	2	1	1	1a	1	2	+	202
815	1	1	1	a	2	1	1	1b	1	2	+	193

[a] Body weights were inadvertently not collected on the day FOB evaluations were performed; body weight data were collected on Study Day -2.

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Males: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
836	2	1	2	1	1	2	1	1	35.7	1	1
837	2	1	2	1	1	2	1	1	36.0	1	1
838	2	1	2	1	1	2	1	1	35.2	1	1
839	2	1	2	1	1	2	1	1	35.5	1	1
840	2	1	2	1	1	1	1	1	34.2	1	1
841	2	1	2	1	1	2	1	1	35.7	1	1
842	2	1	2	1	1	2	1	1	36.3	1	1
843	2	1	2	1	1	2	1	1	35.2	1	1
844	2	1	2	1	1	2	1	1	35.5	1	1
845	2	1	2	1	1	2	1	1	36.4	1	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Males: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g) [a]
836	1	1	1	a	2	1	1	1b	1	2	+	208
837	1	1	1	a	2	1	1	1a	1	2	+	199
838	1	1	1	a	2	1	1	1a	1	2	+	201
839	1	1	1	a	2	1	1	1b	1	2	+	194
840	1	1	1	a	2	1	1	1b	1	2	+	199
841	1	1	1	a	2	1	1	1b	1	2	+	203
842	1	1	1	a	2	1	1	1b	1	2	+	202
843	1	1	1	a	2	1	1	1b	1	2	+	193
844	1	1	1	a	2	1	1	1b	1	2	+	201
845	1	1	1	a	2	1	1	1b	1	2	+	204

[a] Body weights were inadvertently not collected on the day FOB evaluations were performed; body weight data were collected on Study Day -2.

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Males: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
866	2	1	2	1	1	2	1	1	35.5	1	1
867	2	1	2	1	1	2	1	1	35.5	1	1
868	2	1	2	1	1	2	1	1	34.9	1	1
869	2	1	2	1	1	2	1	1	35.1	1	1
870	2	1	2	1	1	2	1	1	35.1	1	1
871	2	1	2	1	1	2	1	1	35.5	1	1
872	3	1	2	1	1	1	1	1	35.1	1	1
873	2	1	2	1	1	2	1	1	35.8	1	1
874	2	1	2	1	1	2	1	1	35.2	1	1
875	2	1	2	1	1	1	1	1	35.6	1	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Males: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g) [a]
866	1	1	1	a	2	1	1	1a	1	2	+	200
867	1	1	1	a	2	1	1	1b	1	2	+	191
868	1	1	1	a	2	1	1	1b	1	2	+	193
869	1	1	1	a	2	1	1	1b	1	2	+	195
870	1	1	1	a	2	1	1	1b	1	2	+	199
871	1	1	1	a	2	1	1	1b	1	2	+	204
872	1	1	1	a	2	1	1	1a	1	2	+	202
873	1	1	1	a	2	1	1	1b	1	2	+	207
874	1	1	1	a	2	1	1	1a	1	2	+	204
875	1	1	1	a	2	1	1	1b	1	2	+	201

[a] Body weights were inadvertently not collected on the day FOB evaluations were performed; body weight data were collected on Study Day -2.

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Females: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day -1 (Pre-Study)

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
821	2	1	2	1	1	2	1	1	35.6	1	1
822	2	1	2	1	1	2	1	1	36.2	1	1
823	2	1	2	1	1	2	1	1	36.2	1	1
824	2	1	2	1	1	2	1	1	34.4	1	1
825	2	1	2	1	1	2	1	1	36.3	1	1
826	2	1	2	1	1	3	1	1	35.9	1	1
827	2	1	2	1	1	2	1	1	35.9	1	1
828	2	1	2	1	1	2	1	1	35.0	1	1
829	2	1	2	1	1	2	1	1	35.9	1	1
830	2	1	2	1	1	2	1	1	35.9	1	1

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Females: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day -1 (Pre-Study)

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g) [a]
821	1	1	1	a	2	1	1	1b	1	2	+	142
822	1	1	1	a	2	1	1	1a	1	2	+	146
823	1	1	1	a	2	1	1	1b	1	2	+	135
824	1	1	1	a	2	1	1	1b	1	2	+	145
825	1	1	1	a	2	1	1	1a	1	2	+	136
826	1	1	1	a	2	1	1	1a	1	2	+	145
827	1	1	1	a	2	1	1	1a	1	2	+	144
828	1	1	1	a	2	1	1	1a	1	2	+	148
829	1	1	1	a	2	1	1	1a	1	2	+	140
830	1	1	1	a	2	1	1	1a	1	2	+	138

[a] Body weights were inadvertently not collected on the day FOB evaluations were performed; body weight data were collected on Study Day -2.

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Females: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
851	2	1	2	1	1	2	1	1	36.1	1	1
852	2	1	2	1	1	2	1	1	36.0	1	1
853	2	1	2	1	1	2	1	1	34.9	1	1
854	2	1	2	1	1	2	1	1	35.0	1	1
855	2	1	2	1	1	2	1	1	35.5	1	1
856	2	1	2	1	1	3	1	1	36.5	1	1
857	2	1	2	1	1	2	1	1	34.8	1	1
858	4	1	2	1	1	2	3	1	36.7	1	1
859	2	1	2	1	1	1	1	1	36.3	1	1
860	2	1	2	1	1	2	1	1	36.2	1	1

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Females: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g) [a]
851	1	1	1	a	2	1	1	1b	1	2	+	144
852	1	1	1	a	2	1	1	1b	1	2	+	140
853	1	1	1	a	2	1	1	1b	1	2	+	138
854	1	1	1	a	2	1	1	1a	1	2	+	142
855	1	1	1	a	2	1	1	1a	1	2	+	137
856	1	1	1	a	2	1	1	1a	1	2	+	140
857	1	1	1	a	2	1	1	1b	1	2	+	134
858	1	1	1	a	2	1	1	1a	1	2	+	146
859	1	1	1	a	2	1	1	1b	1	2	+	146
860	1	1	1	a	2	1	1	1b	1	2	+	148

[a] Body weights were inadvertently not collected on the day FOB evaluations were performed; body weight data were collected on Study Day -2.

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Females: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
881	2	1	2	1	1	2	1	1	36.0	1	1
882	2	1	2	1	1	2	1	1	36.0	1	1
883	2	1	2	1	1	2	1	1	34.8	1	1
884	2	1	2	1	1	2	3	1	36.3	1	1
885	2	1	2	1	1	2	1	1	36.2	1	1
886	2	1	2	1	1	2	1	1	36.1	1	1
887	2	1	2	1	1	3	1	1	36.6	1	1
888	2	1	2	1	1	2	1	1	36.1	1	1
889	2	1	2	1	1	2	1	1	36.0	1	1
890	2	1	2	1	1	2	3	1	36.2	1	1

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Females: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day -1 (Pre-Study)

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g) [a]
881	1	1	1	a	2	1	1	1a	1	2	+	149
882	1	1	1	a	2	1	1	1b	1	2	+	142
883	1	1	1	a	2	1	1	1a	1	2	+	136
884	1	1	1	a	2	1	1	1a	1	2	+	138
885	1	1	1	a	2	1	1	1b	1	2	+	140
886	1	1	1	a	2	1	1	1a	1	2	+	138
887	1	1	1	a	2	1	1	1a	1	2	+	140
888	1	1	1	a	2	1	1	1b	1	2	+	141
889	1	1	1	a	2	1	1	1a	1	2	+	144
890	1	1	1	a	2	1	1	1b	1	2	+	147

[a] Body weights were inadvertently not collected on the day FOB evaluations were performed; body weight data were collected on Study Day -2.

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Males: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 14

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
806	2	1	2	1	1	2	1	1	34.9	1	1
807	2	1	2	1	1	2	1	1	34.5	1	1
808	2	1	2	1	1	2	1	1	34.1	1	1
809	2	1	2	1	1	2	1	1	34.1	1	1
810	2	1	2	1	1	2	1	1	34.3	1	1
811	2	1	2	1	1	2	1	1	34.6	1	1
812	2	1	2	1	1	2	1	1	33.8	1	1
813	2	1	2	1	1	2	1	1	34.5	1	1
814	2	1	2	1	1	2	1	1	34.5	1	1
815	2	1	2	1	1	2	1	1	33.9	1	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Males: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 14

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
806	1	1	1	a	2	1	1	1a	1	2	+	241
807	1	1	1	a	2	1	1	1b	1	2	+	241
808	1	1	1	a	2	1	1	1a	1	2	+	228
809	1	1	1	a	2	1	1	1b	1	2	+	244
810	1	1	1	a	2	1	1	1a	1	2	+	243
811	1	1	1	a	2	1	1	1a	1	2	+	234
812	1	1	1	a	2	1	1	1a	1	2	+	234
813	1	1	1	a	2	1	1	1a	1	2	+	248
814	1	1	1	a	2	1	1	1a	1	2	+	240
815	1	1	1	a	2	1	1	1b	1	2	+	229

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Males: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
836	3	1	2	1	1	2	1	1	34.0	1	1
837	2	1	2	1	1	2	1	1	34.4	1	1
838	4	1	2	1	1	2	1	1	34.1	1	1
839	3	1	2	1	1	2	1	1	34.4	1	1
840	3	1	2	1	1	2	1	1	33.7	1	1
841	2	1	2	1	1	2	1	1	34.8	1	1
842	2	1	2	1	1	2	1	1	33.5	1	1
843	2	1	2	1	1	1	1	1	34.7	1	1
844	2	1	2	1	1	2	1	1	33.7	1	1
845	3	1	2	1	1	2	1	1	33.7	1	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Males: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
836	1	1	1	a	2	1	1	1a	1	2	+	254
837	1	1	1	a	2	1	1	1b	1	2	+	231
838	1	1	1	a	2	1	1	1a	1	2	+	238
839	1	1	1	a	2	1	1	1b	1	2	+	231
840	1	1	1	a	2	1	1	1b	1	2	+	233
841	1	1	1	a	2	1	1	1b	1	2	+	240
842	1	1	1	a	2	1	1	1b	1	2	+	243
843	1	1	1	a	2	1	1	1b	1	2	+	230
844	1	1	1	a	2	1	1	1b	1	2	+	241
845	1	1	1	a	2	1	1	1b	1	2	+	251

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Males: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
866	3	1	2	1	1	2	1	1	33.9	1	1
867	3	1	2	1	1	2	1	1	33.6	1	1
868	2	1	2	1	1	2	1	1	33.8	1	1
869	2	1	2	1	1	2	1	1	33.1	1	1
870	2	1	2	1	1	2	1	1	33.6	1	1
871	2	1	2	1	1	2	1	1	33.7	1	1
872	2	1	2	1	1	2	1	1	33.8	1	1
873	2	1	2	1	1	2	1	1	33.9	1	1
874	3	1	2	1	1	2	1	1	33.0	1	1
875	2	1	2	1	1	2	1	1	33.6	1	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Males: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
866	1	1	1	a	2	1	1	1b	1	2	+	239
867	1	1	1	a	2	1	1	1b	1	2	+	235
868	1	1	1	a	2	1	1	1a	1	2	+	227
869	1	1	1	a	2	1	1	1b	1	2	+	235
870	1	1	1	a	2	1	1	1a	1	2	+	234
871	1	1	1	a	2	1	1	1b	1	2	+	236
872	1	1	1	a	2	1	1	1a	1	2	+	239
873	1	1	1	a	2	1	1	1b	1	2	+	236
874	1	1	1	a	2	1	1	1b	1	2	+	238
875	1	1	1	a	2	1	1	1a	1	2	+	241

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Females: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 14

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
821	2	1	2	1	1	2	1	1	34.1	1	1
822	2	1	2	1	1	2	1	1	35.6	1	1
823	2	1	2	1	1	2	1	1	35.4	1	1
824	2	1	2	1	1	2	1	1	36.7	1	1
825	2	1	2	1	1	2	1	1	34.8	1	1
826	1	4	2	1	1	2	1	1	34.9	1	1
827	2	1	2	1	1	2	1	1	35.0	1	1
828	3	1	2	1	1	2	1	1	35.9	1	1
829	3	1	2	1	1	2	1	1	35.6	1	1
830	3	1	2	1	1	2	1	1	34.3	1	1

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Females: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 14

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
821	1	1	1	a	2	1	1	1a	1	2	+	154
822	1	1	1	a	2	1	1	1b	1	2	+	159
823	1	1	1	a	2	1	1	1b	1	2	+	153
824	1	1	1	a	2	1	1	1b	1	2	+	160
825	1	1	1	a	2	1	1	1a	1	2	+	152
826	1	1	1	a	2	1	1	1b	1	2	+	159
827	1	1	1	a	1	1	1	1b	1	2	+	160
828	1	1	1	a	2	1	1	1b	1	2	+	166
829	1	1	1	a	2	1	1	1b	1	2	+	157
830	1	1	1	a	2	1	1	1b	1	2	+	155

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Females: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
851	2	1	2	1	1	2	1	1	35.3	1	1
852	2	1	2	1	1	2	1	1	35.7	1	1
853	4	1	2	1	1	2	1	1	36.0	1	1
854	2	1	2	1	1	2	1	1	35.2	2	1
855	2	1	2	1	1	2	1	1	33.2	1	1
856	3	1	2	1	1	2	1	1	34.8	1	1
857	2	1	2	1	1	2	1	1	34.9	1	1
858	2	1	2	1	1	2	1	1	35.0	1	1
859	2	1	2	1	1	2	1	1	35.5	1	1
860	2	1	2	1	1	2	1	1	35.1	1	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Females: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
851	1	1	1	a	2	1	1	1a	1	2	+	166
852	1	1	1	a	2	1	1	1b	1	2	+	155
853	1	1	1	a	2	1	1	1b	1	2	+	152
854	1	1	1	a	2	1	1	1a	1	2	+	158
855	1	1	1	a	2	1	1	1b	1	2	+	152
856	1	1	1	a	2	1	1	1b	1	2	+	157
857	1	1	1	a	2	1	1	1b	1	2	+	147
858	1	1	1	a	2	1	1	1b	1	2	+	157
859	1	1	1	a	2	1	1	1b	1	2	+	165
860	1	1	1	a	2	1	1	1b	1	2	+	165

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Females: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
881	2	1	2	1	1	2	1	1	34.3	1	1
882	2	1	2	1	1	2	1	1	35.0	1	1
883	2	1	2	1	1	2	1	1	35.4	1	1
884	2	1	2	1	1	2	1	1	34.7	1	1
885	2	1	2	1	1	2	1	1	35.2	1	1
886	2	1	2	1	1	2	1	1	35.3	1	1
887	3	1	2	1	1	2	1	1	36.0	1	1
888	2	1	2	1	1	2	1	1	35.8	1	1
889	3	1	2	1	1	2	1	1	36.3	1	1
890	2	1	2	1	1	2	1	1	35.7	1	1

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Females: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 14

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
881	1	1	1	a	2	1	1	1a	1	2	+	162
882	1	1	1	a	2	1	1	1a	1	2	+	154
883	1	1	1	a	2	1	1	1b	1	2	+	157
884	1	1	1	a	2	1	1	1b	1	2	+	151
885	1	1	1	a	2	1	1	1b	1	2	+	153
886	1	1	1	a	2	1	1	1a	1	2	+	148
887	1	1	1	a	2	1	1	1b	1	2	+	153
888	1	1	1	a	2	1	1	1b	1	2	+	159
889	1	1	1	a	2	1	1	1b	1	2	+	151
890	1	1	1	a	2	1	1	1b	1	2	+	165

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Males: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 28

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
811	3	1	2	1	1	2	1	1	34.2	1	1
812	3	1	2	1	1	2	1	1	33.5	1	1
813	3	1	2	1	1	2	1	1	33.8	1	1
814	3	1	2	1	1	2	1	1	32.6	1	1
815	2	1	2	1	1	1	1	1	33.2	1	1

Group 1 Females: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 28

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
826	3	1	2	1	1	2	1	1	34.6	1	1
827	3	1	2	1	1	2	1	1	34.6	1	1
828	3	1	2	1	1	2	1	1	36.5	1	1
829	3	1	2	1	1	2	1	1	35.8	1	1
830	4	1	2	1	1	2	1	1	35.9	1	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 1 Males: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 28

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
811	1	1	1	a	2	1	1	1a	1	2	+	262
812	1	1	1	a	2	1	1	1a	1	2	+	275
813	1	1	1	a	2	1	1	1a	1	2	+	292
814	1	1	1	a	2	1	1	1a	1	2	+	270
815	1	1	1	a	2	1	1	1b	1	2	+	267

Group 1 Females: Vehicle Control (0.000 mg/kg/day CuATSM/H_2ATSM) – Study Day 28

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
826	1	1	1	a	2	1	1	1a	1	2	+	169
827	1	1	1	a	2	1	1	1b	1	2	+	167
828	1	1	1	a	2	1	1	1b	1	2	+	188
829	1	1	1	a	2	1	1	1a	1	2	+	172
830	1	1	1	a	2	1	1	1a	1	2	+	171

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Males: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
841	3	1	2	1	1	2	1	1	33.8	1	1
842	3	1	2	1	1	2	1	1	33.3	1	1
843	3	1	2	1	1	2	1	1	33.7	1	1
844	3	1	2	1	1	2	1	1	33.5	1	1
845	3	1	2	1	1	2	1	1	34.0	1	1

Group 2 Females: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
856	3	1	2	1	1	1	1	1	35.3	2	1
857	3	1	2	1	1	2	1	1	34.9	1	1
858	3	1	2	1	1	2	1	1	34.0	1	1
859	3	1	2	1	1	2	1	1	34.6	1	1
860	3	1	2	1	1	2	2	1	34.2	1	1

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 2 Males: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
841	1	1	1	a	2	1	1	1b	1	2	+	276
842	1	1	1	a	2	1	1	1a	1	2	+	283
843	1	1	1	a	2	1	1	1b	1	2	+	273
844	1	1	1	a	2	1	1	1a	1	2	+	282
845	1	1	1	a	2	1	1	1b	1	2	+	290

Group 2 Females: 0.075 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
856	1	1	1	a	2	1	1	1a	1	2	+	171
857	1	1	1	a	2	1	1	1a	1	2	+	160
858	1	1	1	a	2	1	1	1a	1	2	+	171
859	1	1	1	a	2	1	1	1b	1	2	+	183
860	1	1	1	a	2	1	1	1b	1	2	+	182

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Males: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
871	3	1	2	1	1	1	1	1	34.6	1	1
872	3	1	2	1	1	2	1	1	35.1	1	1
873	3	1	2	1	1	1	1	1	35.0	1	1
874	3	1	2	1	1	2	1	1	35.7	1	1
875	3	1	2	1	1	2	1	1	34.9	1	1

Group 3 Females: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Posture	Palpebral Closure	Convulsions or Tremors	Biting	Vocalizations	Reflexes	Ease of Removal	Ease of Handling	Body Temp (°C)	Lacrimation	Salivation
886	3	1	2	1	1	2	1	1	35.5	1	1
887	3	1	2	1	1	2	1	1	36.1	1	1
888	3	1	2	1	1	2	1	1	36.0	1	1
889	3	1	2	1	1	2	1	1	35.8	2	1
890	3	1	2	1	1	2	1	1	35.8	2	1

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-6 (cont.)

Individual Animal Functional Observational Battery Observations

Group 3 Males: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
871	1	1	1	a	2	1	1	1a	1	2	+	261
872	1	1	1	a	2	1	1	1a	1	2	+	281
873	1	1	1	a	2	1	1	1a	1	2	+	272
874	1	1	1	a	2	1	1	1a	1	2	+	275
875	1	1	1	a	2	1	1	1b	1	2	+	273

Group 3 Females: 0.150 mg/kg/day CuATSM/H_2ATSM – Study Day 28

Animal Number	Fur Appearance	Gait Description	Diarrhea	Urine	Tail Pinch	Pupil Response	Eye Blink Response	Vision	Hindlimb Extension	Catalepsy	Righting Reflex	Body Weight (g)
886	1	1	1	a	2	1	1	1b	1	2	+	159
887	1	1	1	a	2	1	1	1b	1	2	+	172
888	1	1	1	a	2	1	1	1b	1	2	+	177
889	1	1	1	a	2	1	1	1b	1	2	+	169
890	1	1	1	a	2	1	1	1b	1	2	+	181

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
806	145	5.1	94	415	66	89	0.31	16	0.4
807	144	5.2	96	394	68	95	0.27	18	0.4
808	148	5.4	97	369	48	84	0.24	19	0.4
809	145	5.1	95	380	46	71	0.38	16	0.4
810	146	5.2	96	345	43	77	0.34	14	0.4
811	145	5.0	99	338	49	69	0.33	18	0.5
812	144	5.3	98	340	46	76	0.27	17	0.4
813	146	5.1	98	366	68	99	0.40	16	0.4
814	145	5.2	100	361	74	111	0.32	16	0.4
815	146	5.2	97	350	49	68	0.30	15	0.4
MEAN	145	5.2	97	366	56	84	0.32	17	0.4
SD	1.2	0.11	1.8	24.9	11.7	14.4	0.050	1.5	0.03
N	10	10	10	10	10	10	10	10	10
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
836	147	5.7	94	384	51	72	0.34	17	0.4
837	146	5.2	96	376	49	113	0.29	17	0.4
838	146	5.3	96	375	47	70	0.35	18	0.4
839	144	5.6	99	364	53	115	0.27	20	0.4
840	145	5.3	99	373	46	84	0.30	18	0.4
841	144	5.5	98	418	52	85	0.39	18	0.3
842	145	5.0	95	368	47	69	0.35	17	0.4
843	146	5.2	95	383	50	78	0.35	17	0.4
844	144	5.6	101	337	49	82	0.37	17	0.4
845	145	5.0	99	340	46	75	0.37	15	0.4
MEAN	145	5.3	97	372	49	84	0.34	17	0.4
SD	1.0	0.25	2.3	22.9	2.5	16.6	0.039	1.3	0.03
N	10	10	10	10	10	10	10	10	10

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: MALE

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
806	114	5.8	4.1	1.7	2.4	48	137	11.2	11.3
807	132	5.9	4.0	1.9	2.1	43	123	11.0	11.5
808	133	5.7	4.1	1.6	2.6	39	87	11.3	11.4
809	137	5.8	4.0	1.8	2.2	39	122	11.3	11.4
810	124	6.0	4.0	2.0	2.0	36	165	10.9	11.4
811	139	6.0	4.0	2.0	2.0	39	147	11.1	11.0
812	140	5.8	3.9	1.9	2.1	44	117	11.1	11.8
813	142	5.7	4.0	1.7	2.4	35	147	11.2	12.4
814	136	5.6	3.9	1.7	2.3	35	125	10.8	11.1
815	132	5.7	3.9	1.8	2.2	42	112	11.1	11.4
MEAN	133	5.8	4.0	1.8	2.2	40	128	11.1	11.5
SD	8.4	0.13	0.07	0.14	0.19	4.2	21.9	0.16	0.39
N	10	10	10	10	10	10	10	10	10
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
836	126	5.9	4.2	1.7	2.5	48	148	11.4	11.7
837	122	6.1	4.3	1.8	2.4	41	127	11.1	11.1
838	123	5.7	4.0	1.7	2.4	41	125	11.1	11.1
839	155	5.9	4.1	1.8	2.3	43	134	11.4	12.8
840	127	6.0	4.1	1.9	2.2	42	171	11.0	11.9
841	132	5.8	4.0	1.8	2.2	44	80	10.8	11.5
842	150	5.7	3.8	1.9	2.0	41	128	11.2	12.1
843	139	6.0	4.0	2.0	2.0	44	92	11.3	12.0
844	135	5.7	4.0	1.7	2.4	35	142	11.0	11.7
845	145	5.6	3.8	1.8	2.1	39	157	11.2	11.9
MEAN	135	5.8	4.0	1.8	2.3	42	130	11.2	11.8
SD	11.6	0.16	0.16	0.10	0.18	3.4	27.6	0.19	0.50
N	10	10	10	10	10	10	10	10	10

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
866	147	5.5	96	396	50	77	0.28	16	0.4
867	147	5.6	95	395	49	70	0.39	19	0.4
868	147	5.2	97	398	56	99	0.38	19	0.4
869	144	5.3	98	359	43	70	0.35	20	0.4
870	145	5.0	98	372	51	86	0.34	18	0.4
871	145	4.9	96	354	49	70	0.35	17	0.5
872	144	5.6	99	407	54	84	0.33	19	0.4
873	145	5.2	96	340	44	70	0.18	17	0.4
874	145	5.2	97	390	48	78	0.34	18	0.4
875	144	5.1	98	335	95	131	0.49	15	0.3
MEAN	145	5.3	97	375	54	84	0.34	18	0.4
SD	1.3	0.24	1.2	26.1	15.0	19.2	0.079	1.5	0.05
N	10	10	10	10	10	10	10	10	10

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: MALE

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
866	123	5.9	4.0	1.9	2.1	43	136	11.1	11.3
867	122	6.0	4.1	1.9	2.2	45	119	11.5	11.9
868	122	6.0	4.2	1.8	2.3	42	167	11.5	12.0
869	156	5.8	3.8	2.0	1.9	36	164	11.3	13.4
870	135	5.9	3.9	2.0	2.0	41	137	10.8	10.8
871	163	5.9	4.0	1.9	2.1	41	128	11.2	11.3
872	129	6.2	4.2	2.0	2.1	47	105	11.1	11.9
873	129	5.6	4.0	1.6	2.5	36	136	11.0	11.0
874	135	5.9	4.0	1.9	2.1	39	156	11.3	11.7
875	134	5.6	3.9	1.7	2.3	36	86	10.8	10.8
MEAN	135	5.9	4.0	1.9	2.2	41	133	11.2	11.6
SD	14.1	0.18	0.13	0.13	0.17	3.9	25.6	0.25	0.78
N	10	10	10	10	10	10	10	10	10

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
821	144	5.2	101	347	46	73	0.25	18	0.3
822	146	4.7	98	291	38	66	0.34	15	0.3
823	145	4.4	98	295	39	69	0.30	14	0.4
824	145	5.1	100	298	48	96	0.36	16	0.4
825	145	4.5	98	330	47	73	0.31	17	0.4
826	146	4.8	96	289	39	63	0.34	16	0.4
827	145	4.9	100	340	44	97	0.35	18	0.3
828	147	4.8	99	352	41	74	0.44	19	0.4
829	146	4.9	97	341	44	74	0.26	17	0.4
830	147	4.6	96	323	49	74	0.33	17	0.4
MEAN	146	4.8	98	321	44	76	0.33	17	0.4
SD	1.0	0.25	1.7	25.0	4.0	11.5	0.054	1.5	0.05
N	10	10	10	10	10	10	10	10	10
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
851	144	5.4	102	316	43	80	0.29	16	0.4
852	144	4.7	99	346	43	79	0.34	15	0.4
853	144	4.7	99	302	41	74	0.35	13	0.4
854	143	5.3	101	355	45	114	0.37	17	0.3
855	147	4.7	97	341	46	70	0.55	17	0.4
856	145	4.6	98	288	36	69	0.27	14	0.4
857	146	4.6	99	317	36	65	0.33	15	0.4
858	147	4.8	96	274	38	98	0.35	14	0.3
859	146	4.8	99	300	40	69	0.34	14	0.4
860	144	4.7	95	321	43	85	0.25	14	0.4
MEAN	145	4.8	99	316	41	80	0.34	15	0.4
SD	1.4	0.28	2.1	26.0	3.5	15.3	0.082	1.4	0.04
N	10	10	10	10	10	10	10	10	10

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
821	126	5.4	4.0	1.4	2.9	72	107	10.8	11.3
822	115	5.6	3.9	1.7	2.3	62	110	10.7	9.4
823	142	5.2	3.7	1.5	2.5	53	68	10.8	10.8
824	140	5.7	3.9	1.8	2.2	53	75	10.8	11.3
825	132	5.4	3.7	1.7	2.2	50	77	10.7	11.2
826	144	5.3	3.8	1.5	2.5	53	79	11.2	12.0
827	130	5.5	3.8	1.7	2.2	60	101	10.8	11.0
828	147	5.4	3.9	1.5	2.6	54	72	11.2	11.1
829	134	5.6	4.0	1.6	2.5	46	87	11.1	11.6
830	133	5.6	3.8	1.8	2.1	48	94	11.2	11.5
MEAN	134	5.5	3.9	1.6	2.4	55	87	10.9	11.1
SD	9.5	0.16	0.11	0.14	0.24	7.7	15.2	0.22	0.69
N	10	10	10	10	10	10	10	10	10
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
851	142	5.6	3.7	1.9	1.9	50	80	10.8	11.6
852	140	5.5	3.8	1.7	2.2	61	89	10.9	11.1
853	130	5.2	3.7	1.5	2.5	56	63	10.4	9.9
854	138	5.7	3.9	1.8	2.2	52	86	10.8	11.5
855	113	5.8	4.0	1.8	2.2	58	101	11.0	10.8
856	134	5.5	3.8	1.7	2.2	53	73	10.8	11.2
857	139	5.4	3.8	1.6	2.4	56	85	11.0	12.0
858	122	5.2	3.9	1.3	3.0	52	72	10.7	10.5
859	134	5.9	3.9	2.0	2.0	59	73	11.0	10.6
860	133	5.5	3.7	1.8	2.1	56	79	10.9	11.4
MEAN	133	5.5	3.8	1.7	2.3	55	80	10.8	11.1
SD	8.9	0.23	0.10	0.20	0.31	3.5	10.7	0.18	0.62
N	10	10	10	10	10	10	10	10	10

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
881	144	4.6	101	348	44	87	0.27	16	0.3
882	145	4.8	98	294	41	70	0.29	16	0.4
883	145	4.9	101	308	47	93	0.24	16	0.9
884	145	4.7	99	319	46	77	0.39	15	0.4
885	146	4.4	97	317	46	81	0.39	14	0.4
886	144	4.6	100	333	42	70	0.28	16	0.4
887	146	4.7	98	321	44	78	0.31	17	0.4
888	146	4.8	98	333	44	74	0.30	13	0.4
889	147	5.2	98	286	44	91	0.38	14	0.4
890	144	4.4	96	320	45	65	0.34	15	0.4
MEAN	145	4.7	99	318	44	79	0.32	15	0.4
SD	1.0	0.24	1.6	18.5	1.8	9.4	0.053	1.2	0.16
N	10	10	10	10	10	10	10	10	10

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
881	123	5.3	3.8	1.5	2.5	51	102	10.5	10.0
882	132	5.4	3.6	1.8	2.0	56	66	10.6	11.3
883	134	5.6	3.9	1.7	2.3	56	80	11.1	12.4
884	125	5.6	3.8	1.8	2.1	51	60	10.7	10.1
885	130	5.4	3.9	1.5	2.6	53	84	10.8	10.7
886	138	5.5	3.8	1.7	2.2	47	74	10.9	11.5
887	144	5.6	3.9	1.7	2.3	57	99	11.0	11.7
888	126	5.4	3.8	1.6	2.4	50	69	10.8	10.6
889	152	5.6	4.0	1.6	2.5	50	56	11.1	11.7
890	135	5.4	3.7	1.7	2.2	56	66	11.1	11.5
MEAN	134	5.5	3.8	1.7	2.3	53	76	10.9	11.2
SD	9.0	0.11	0.11	0.11	0.19	3.4	15.6	0.22	0.77
N	10	10	10	10	10	10	10	10	10

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
806	143	4.6	94	236	46	90	0.18	10	0.4
807	144	4.7	96	246	46	84	0.12	11	0.5
808	144	5.0	96	222	44	86	0.14	10	0.6
809	141	4.6	96	250	45	85	0.24	12	0.4
810	142	4.9	98	253	42	86	0.10	11	0.4
MEAN	143	4.8	96	241	45	86	0.16	11	0.5
SD	1.3	0.18	1.4	12.6	1.7	2.3	0.055	0.8	0.09
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
811	143	5.3	95	346	43	69	0.17	15	0.4
812	143	5.1	96	342	42	72	0.10	13	0.5
813	143	5.3	95	329	61	88	0.00	15	0.5
814	141	4.9	96	361	56	85	0.26	17	0.4
815	144	5.1	95	346	45	75	0.09	15	0.4
MEAN	143	5.1	95	345	49	78	0.12	15	0.4
SD	1.1	0.17	0.5	11.4	8.6	8.3	0.097	1.4	0.05
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
806	120	5.8	4.0	1.8	2.2	36	61	10.7	10.1
807	132	6.0	4.0	2.0	2.0	32	55	10.7	9.8
808	115	5.7	4.0	1.7	2.4	33	49	10.8	10.8
809	129	5.9	3.9	2.0	2.0	33	39	10.8	10.6
810	125	5.7	3.8	1.9	2.0	26	27	10.5	10.7
MEAN	124	5.8	3.9	1.9	2.1	32	46	10.7	10.4
SD	6.8	0.13	0.09	0.13	0.18	3.7	13.5	0.12	0.43
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
811	118	6.2	4.1	2.1	2.0	37	142	11.3	9.6
812	137	5.9	3.9	2.0	2.0	35	131	11.4	10.9
813	127	5.8	4.0	1.8	2.2	34	161	11.2	10.6
814	137	5.9	4.1	1.8	2.3	36	142	11.1	10.4
815	138	5.7	3.8	1.9	2.0	37	127	11.3	11.1
MEAN	131	5.9	4.0	1.9	2.1	36	141	11.3	10.5
SD	8.7	0.19	0.13	0.13	0.14	1.3	13.2	0.11	0.58
N	5	5	5	5	5	5	5	5	5

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
836	143	4.8	97	232	42	87	0.20	10	0.5
837	142	4.7	98	217	59	114	0.06	12	0.6
838	143	4.8	96	231	47	86	0.09	11	0.4
839	142	4.3	98	218	39	72	0.26	12	0.5
840	140	4.5	97	234	42	81	0.10	10	0.4
MEAN	142	4.6	97	226	46	88	0.14	11	0.5
SD	1.2	0.22	0.8	8.2	7.9	15.7	0.084	1.0	0.08
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
841	143	5.4	93	374	45	71	0.16	16	0.5
842	144	5.3	94	317	39	72	0.10	14	0.5
843	144	5.0	94	369	57	86	0.12	17	0.4
844	143	5.1	98	355	53	90	0.02	18	0.4
845	142	5.0	96	356	78	109	0.16	17	0.4
MEAN	143	5.2	95	354	54	86	0.11	16	0.4
SD	0.8	0.18	2.0	22.4	14.9	15.5	0.058	1.5	0.05
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
836	123	5.8	3.9	1.9	2.1	36	91	10.8	10.4
837	108	5.8	3.9	1.9	2.1	29	66	10.5	10.2
838	127	5.8	3.9	1.9	2.1	34	62	10.5	10.3
839	127	5.7	3.9	1.8	2.2	30	49	10.6	10.7
840	117	5.8	3.8	2.0	1.9	33	76	10.6	10.6
MEAN	120	5.8	3.9	1.9	2.1	32	69	10.6	10.4
SD	8.0	0.04	0.04	0.07	0.11	2.9	15.7	0.12	0.21
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
841	134	6.0	4.0	2.0	2.0	40	132	11.3	10.6
842	130	6.1	4.0	2.1	1.9	38	152	11.5	10.9
843	139	5.8	4.0	1.8	2.2	41	164	11.5	11.2
844	130	5.8	3.9	1.9	2.1	38	173	11.5	11.2
845	135	5.8	4.0	1.8	2.2	39	129	11.3	10.7
MEAN	134	5.9	4.0	1.9	2.1	39	150	11.4	10.9
SD	3.8	0.14	0.04	0.13	0.13	1.3	19.3	0.11	0.28
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
866	140	4.7	97	248	48	93	0.06	15	0.5
867	145	5.4	93	278	49	92	0.13	11	0.5
868	142	4.8	96	256	55	93	0.12	9	0.4
869	143	5.0	95	253	48	95	0.19	12	0.4
870	143	4.9	95	222	43	77	0.19	9	0.5
MEAN	143	5.0	95	251	49	90	0.14	11	0.5
SD	1.8	0.27	1.5	20.0	4.3	7.3	0.054	2.5	0.05
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
871	140	5.0	97	322	51	94	0.18	16	0.5
872	143	5.2	95	359	70	102	0.05	15	0.5
873	143	5.7	93	327	51	78	0.12	14	0.4
874	143	4.9	96	358	47	73	0.21	18	0.4
875	142	5.2	96	356	54	88	0.14	14	0.4
MEAN	142	5.2	95	344	55	87	0.14	15	0.4
SD	1.3	0.31	1.5	18.3	9.0	11.7	0.061	1.7	0.05
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Males

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
866	119	5.9	3.9	2.0	2.0	37	66	10.7	10.8
867	117	6.2	4.1	2.1	2.0	39	95	11.3	11.1
868	113	5.9	4.0	1.9	2.1	32	80	10.8	10.5
869	117	5.9	4.0	1.9	2.1	33	83	10.9	11.5
870	117	6.1	4.1	2.0	2.1	29	55	11.0	10.5
MEAN	117	6.0	4.0	2.0	2.1	34	76	10.9	10.9
SD	2.2	0.14	0.08	0.08	0.05	4.0	15.5	0.23	0.43
N	5	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
871	188	6.1	4.0	2.1	1.9	38	155	11.8	11.6
872	136	5.8	4.0	1.8	2.2	41	213	11.3	10.5
873	125	6.0	4.0	2.0	2.0	40	178	11.2	10.3
874	132	5.9	4.1	1.8	2.3	37	166	11.5	11.3
875	128	5.9	4.1	1.8	2.3	37	102	11.3	10.3
MEAN	142	5.9	4.0	1.9	2.1	39	163	11.4	10.8
SD	26.2	0.11	0.05	0.14	0.18	1.8	40.4	0.24	0.61
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
821	143	4.5	97	196	42	95	0.13	10	0.4
822	144	4.5	98	156	35	72	0.32	10	0.5
823	142	4.1	100	187	36	84	0.26	16	0.4
824	140	5.1	103	176	43	123	0.22	15	0.4
825	141	4.3	101	193	43	82	0.19	12	0.4
MEAN	142	4.5	100	182	40	91	0.22	13	0.4
SD	1.6	0.37	2.4	16.2	4.0	19.6	0.072	2.8	0.04
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
826	143	4.4	97	280	35	69	0.18	16	0.4
827	141	4.8	100	301	35	72	0.21	15	0.4
828	142	4.9	96	324	34	69	0.17	14	0.4
829	141	4.8	99	276	35	69	0.18	10	0.3
830	140	4.4	99	281	39	74	0.13	13	0.4
MEAN	141	4.7	98	292	36	71	0.17	14	0.4
SD	1.1	0.24	1.6	20.2	1.9	2.3	0.029	2.3	0.04
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
821	100	5.9	4.1	1.8	2.3	52	44	10.6	9.0
822	88	5.8	4.0	1.8	2.2	51	41	10.6	8.4
823	95	5.8	4.1	1.7	2.4	44	34	10.4	8.5
824	113	5.9	4.0	1.9	2.1	45	31	10.5	9.7
825	110	5.6	3.9	1.7	2.3	40	27	10.3	8.6
MEAN	101	5.8	4.0	1.8	2.3	46	35	10.5	8.8
SD	10.4	0.12	0.08	0.08	0.11	5.0	7.0	0.13	0.53
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
826	143	5.5	3.9	1.6	2.4	54	70	11.1	10.1
827	136	5.8	3.9	1.9	2.1	50	70	10.8	9.8
828	137	5.7	3.9	1.8	2.2	50	57	11.1	9.6
829	125	5.7	3.8	1.9	2.0	43	39	10.8	8.5
830	134	5.4	3.7	1.7	2.2	49	70	10.9	10.3
MEAN	135	5.6	3.8	1.8	2.2	49	61	10.9	9.7
SD	6.5	0.16	0.09	0.13	0.15	4.0	13.6	0.15	0.70
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
851	143	4.5	99	202	35	77	0.22	13	0.4
852	139	4.6	99	180	37	89	0.18	9	0.4
853	141	4.5	100	176	36	79	0.00	13	0.4
854	143	4.8	102	186	41	84	0.26	15	0.4
855	142	4.5	101	180	39	82	0.21	13	0.4
MEAN	142	4.6	100	185	38	82	0.17	13	0.4
SD	1.7	0.13	1.3	10.3	2.4	4.7	0.101	2.2	0.00
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
856	139	4.8	100	359	36	75	0.20	18	0.4
857	140	4.4	101	304	43	77	0.06	14	0.4
858	144	4.9	99	293	39	69	0.18	19	0.4
859	141	4.4	100	326	35	70	0.17	19	0.4
860	142	4.4	98	334	39	80	0.21	15	0.4
MEAN	141	4.6	100	323	38	74	0.16	17	0.4
SD	1.9	0.25	1.1	25.9	3.1	4.7	0.060	2.3	0.00
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
851	108	5.6	3.8	1.8	2.1	41	32	10.5	9.4
852	111	5.6	3.8	1.8	2.1	45	54	10.4	8.5
853	109	5.6	4.0	1.6	2.5	43	41	10.4	9.5
854	129	5.6	3.8	1.8	2.1	43	34	10.7	10.6
855	115	5.7	3.9	1.8	2.2	46	36	10.4	9.3
MEAN	114	5.6	3.9	1.8	2.2	44	39	10.5	9.5
SD	8.6	0.04	0.09	0.09	0.17	1.9	8.8	0.13	0.75
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
856	134	5.8	4.0	1.8	2.2	48	123	11.1	10.5
857	132	5.3	3.6	1.7	2.1	45	74	10.9	10.4
858	113	5.9	4.2	1.7	2.5	51	76	11.2	8.7
859	136	5.9	3.8	2.1	1.8	44	61	10.9	10.2
860	121	6.0	4.0	2.0	2.0	48	88	11.1	10.3
MEAN	127	5.8	3.9	1.9	2.1	47	84	11.0	10.0
SD	9.8	0.28	0.23	0.18	0.26	2.8	23.6	0.13	0.75
N	5	5	5	5	5	5	5	5	5

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
881	140	4.2	100	211	37	92	0.19	12	0.4
882	142	4.4	99	172	35	77	0.18	15	0.5
883	142	4.5	97	179	49	87	0.21	13	0.4
884	144	4.3	99	178	45	85	0.18	13	0.4
885	140	4.6	103	166	38	85	0.14	10	0.3
MEAN	142	4.4	100	181	41	85	0.18	13	0.4
SD	1.7	0.16	2.2	17.5	5.9	5.4	0.025	1.8	0.07
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
886	144	4.3	98	290	47	91	0.05	16	0.4
887	141	5.4	100	220	40	80	0.10	13	0.4
888	141	4.6	99	338	33	73	0.14	15	0.4
889	142	4.5	100	298	36	73	0.20	13	0.4
890	139	5.4	102	276	38	77	0.11	13	0.4
MEAN	141	4.8	100	284	39	79	0.12	14	0.4
SD	1.8	0.52	1.5	42.7	5.3	7.4	0.055	1.4	0.00
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 15

Fasted Females

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
881	100	5.7	4.0	1.7	2.4	45	46	10.2	8.3
882	107	5.8	3.8	2.0	1.9	45	48	10.6	9.5
883	104	5.8	3.9	1.9	2.1	41	28	10.6	9.5
884	104	5.6	4.0	1.6	2.5	47	25	10.6	8.5
885	111	5.5	3.8	1.7	2.2	39	30	10.5	9.5
MEAN	105	5.7	3.9	1.8	2.2	43	35	10.5	9.1
SD	4.1	0.13	0.10	0.16	0.24	3.3	10.8	0.17	0.61
N	5	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
886	146	5.7	3.8	1.9	2.0	43	68	10.9	9.2
887	160	5.1	3.4	1.7	2.0	41	51	11.0	10.9
888	129	5.6	3.7	1.9	1.9	48	80	10.8	9.5
889	139	5.3	3.7	1.6	2.3	49	74	10.9	10.2
890	155	5.3	3.6	1.7	2.1	46	90	11.3	11.5
MEAN	146	5.4	3.6	1.8	2.1	45	73	11.0	10.3
SD	12.4	0.24	0.15	0.13	0.15	3.4	14.6	0.19	0.96
N	5	5	5	5	5	5	5	5	5

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE
STUDY NO: 2073022

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
806	a	a	a	a	a	a	a	a	a
807	a	a	a	a	a	a	a	a	a
808	a	a	a	a	a	a	a	a	a
809	a	a	a	a	a	a	a	a	a
810	a	a	a	a	a	a	a	a	a
811	141	5.5	104	176	46	86	0.37	15	0.4
812	143	4.6	99	179	43	81	0.46	14	0.5
813	145	5.0	99	163	42	86	0.46	13	0.4
814	145	4.4	95	172	40	80	0.45	12	0.4
815	143	4.9	99	169	39	71	0.30	11	0.4
MEAN	143	4.9	99	172	42	81	0.41	13	0.4
SD	1.7	0.42	3.2	6.2	2.7	6.1	0.071	1.6	0.04
N	5	5	5	5	5	5	5	5	5
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
836	a	a	a	a	a	a	a	a	a
837	a	a	a	a	a	a	a	a	a
838	a	a	a	a	a	a	a	a	a
839	a	a	a	a	a	a	a	a	a
840	a	a	a	a	a	a	a	a	a
841	145	4.8	98	184	43	85	0.37	15	0.4
842	143	4.9	101	145	38	76	0.45	11	0.4
843	147	4.3	96	176	53	91	0.36	11	0.5
844	143	5.1	100	151	41	79	0.35	15	0.4
845	144	4.9	100	142	43	83	0.40	12	0.4
MEAN	144	4.8	99	160	44	83	0.39	13	0.4
SD	1.7	0.30	2.0	19.1	5.6	5.8	0.040	2.0	0.04
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: MALE

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
806	a	a	a	a	a	a	a	a	a
807	a	a	a	a	a	a	a	a	a
808	a	a	a	a	a	a	a	a	a
809	a	a	a	a	a	a	a	a	a
810	a	a	a	a	a	a	a	a	a
811	132	5.9	4.2	1.7	2.5	21	44	10.2	9.5
812	120	5.9	3.9	2.0	2.0	22	60	10.4	9.7
813	131	5.9	4.0	1.9	2.1	26	76	10.7	10.5
814	118	6.1	4.2	1.9	2.2	23	37	10.6	9.9
815	119	5.8	4.1	1.7	2.4	27	64	10.6	10.2
MEAN	124	5.9	4.1	1.8	2.2	24	56	10.5	10.0
SD	6.9	0.11	0.13	0.13	0.21	2.6	15.7	0.20	0.40
N	5	5	5	5	5	5	5	5	5
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM									
836	a	a	a	a	a	a	a	a	a
837	a	a	a	a	a	a	a	a	a
838	a	a	a	a	a	a	a	a	a
839	a	a	a	a	a	a	a	a	a
840	a	a	a	a	a	a	a	a	a
841	134	6.2	4.2	2.0	2.1	30	116	10.6	9.2
842	128	5.7	4.0	1.7	2.4	22	59	10.7	10.4
843	120	6.2	4.4	1.8	2.4	26	86	10.9	9.7
844	140	5.8	4.0	1.8	2.2	28	94	10.7	10.6
845	116	5.6	3.8	1.8	2.1	24	62	10.6	11.0
MEAN	128	5.9	4.1	1.8	2.2	26	83	10.7	10.2
SD	9.8	0.28	0.23	0.11	0.15	3.2	23.6	0.12	0.72
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
866	a	a	a	a	a	a	a	a	a
867	a	a	a	a	a	a	a	a	a
868	a	a	a	a	a	a	a	a	a
869	a	a	a	a	a	a	a	a	a
870	a	a	a	a	a	a	a	a	a
871	142	5.5	102	155	41	80	0.30	14	0.4
872	144	4.6	101	159	45	82	0.38	12	0.4
873	145	4.8	96	157	35	78	0.45	12	0.4
874	148	4.5	99	162	45	85	0.40	11	0.4
875	147	4.9	97	143	38	78	0.55	11	0.4
MEAN	145	4.9	99	155	41	81	0.42	12	0.4
SD	2.4	0.39	2.5	7.3	4.4	3.0	0.092	1.2	0.00
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: MALE

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM									
866	a	a	a	a	a	a	a	a	a
867	a	a	a	a	a	a	a	a	a
868	a	a	a	a	a	a	a	a	a
869	a	a	a	a	a	a	a	a	a
870	a	a	a	a	a	a	a	a	a
871	117	6.2	3.5	2.7	1.3	24	26	10.2	10.4
872	123	5.8	4.1	1.7	2.4	29	94	10.7	9.9
873	113	5.7	4.0	1.7	2.4	27	77	10.6	9.4
874	118	5.7	4.2	1.5	2.8	22	70	10.8	10.0
875	99	5.8	4.0	1.8	2.2	24	36	10.8	10.1
MEAN	114	5.8	4.0	1.9	2.2	25	61	10.6	10.0
SD	9.1	0.21	0.27	0.47	0.56	2.8	28.6	0.25	0.36
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
821	a	a	a	a	a	a	a	a	a
822	a	a	a	a	a	a	a	a	a
823	a	a	a	a	a	a	a	a	a
824	a	a	a	a	a	a	a	a	a
825	a	a	a	a	a	a	a	a	a
826	147	4.6	100	106	74	143	0.41	15	0.4
827	144	4.7	100	131	35	85	0.41	14	0.4
828	143	4.9	102	137	33	73	0.34	15	0.4
829	146	4.7	99	116	37	78	0.35	12	0.4
830	147	4.5	98	134	41	73	0.43	16	0.4
MEAN	145	4.7	100	125	44	90	0.39	14	0.4
SD	1.8	0.15	1.5	13.3	17.0	29.8	0.040	1.5	0.00
N	5	5	5	5	5	5	5	5	5
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
851	a	a	a	a	a	a	a	a	a
852	a	a	a	a	a	a	a	a	a
853	a	a	a	a	a	a	a	a	a
854	a	a	a	a	a	a	a	a	a
855	a	a	a	a	a	a	a	a	a
856	142	5.1	102	133	33	77	0.36	15	0.3
857	145	5.1	102	122	42	82	0.43	13	0.4
858	146	5.0	99	127	38	81	0.52	12	0.5
859	147	4.7	100	131	35	77	0.36	11	0.4
860	147	4.9	98	139	39	76	0.51	14	0.4
MEAN	145	5.0	100	130	37	79	0.44	13	0.4
SD	2.1	0.17	1.8	6.4	3.5	2.7	0.078	1.6	0.07
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)									
821	a	a	a	a	a	a	a	a	a
822	a	a	a	a	a	a	a	a	a
823	a	a	a	a	a	a	a	a	a
824	a	a	a	a	a	a	a	a	a
825	a	a	a	a	a	a	a	a	a
826	116	5.8	3.8	2.0	1.9	44	16	10.7	9.3
827	104	5.8	3.9	1.9	2.1	40	16	10.4	9.6
828	106	5.9	4.0	1.9	2.1	41	19	10.3	9.5
829	102	5.7	4.1	1.6	2.6	40	14	10.3	9.3
830	108	5.9	3.9	2.0	2.0	39	19	10.8	10.1
MEAN	107	5.8	3.9	1.9	2.1	41	17	10.5	9.6
SD	5.4	0.08	0.11	0.16	0.27	1.9	2.2	0.23	0.33
N	5	5	5	5	5	5	5	5	5
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM									
851	a	a	a	a	a	a	a	a	a
852	a	a	a	a	a	a	a	a	a
853	a	a	a	a	a	a	a	a	a
854	a	a	a	a	a	a	a	a	a
855	a	a	a	a	a	a	a	a	a
856	112	5.6	3.9	1.7	2.3	37	12	10.2	10.0
857	108	5.7	3.8	1.9	2.0	40	25	10.8	11.3
858	87	5.6	3.9	1.7	2.3	42	23	10.3	9.0
859	102	5.7	4.0	1.7	2.4	40	24	10.7	9.2
860	103	6.0	4.2	1.8	2.3	43	20	10.6	9.3
MEAN	102	5.7	4.0	1.8	2.3	40	21	10.5	9.8
SD	9.5	0.16	0.15	0.09	0.15	2.3	5.3	0.26	0.94
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002
STUDY NO: 2073022
SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	BUN mg/dL	CRE mg/dL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
881	a	a	a	a	a	a	a	a	a
882	a	a	a	a	a	a	a	a	a
883	a	a	a	a	a	a	a	a	a
884	a	a	a	a	a	a	a	a	a
885	a	a	a	a	a	a	a	a	a
886	144	5.6	100	113	41	85	0.42	14	0.4
887	144	4.9	102	141	45	87	0.32	16	0.4
888	146	4.6	102	151	35	75	0.47	15	0.4
889	145	4.9	99	141	36	82	0.48	15	0.4
890	146	5.2	100	117	37	78	0.44	11	0.4
MEAN	145	5.0	101	133	39	81	0.43	14	0.4
SD	1.0	0.38	1.3	16.6	4.1	4.9	0.064	1.9	0.00
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE
STUDY NO: 2073022

Animal ID	GLUC mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G RATIO -	CHOL mg/dL	TG mg/dL	CALC mg/dL	PHOS mg/dL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM									
881	a	a	a	a	a	a	a	a	a
882	a	a	a	a	a	a	a	a	a
883	a	a	a	a	a	a	a	a	a
884	a	a	a	a	a	a	a	a	a
885	a	a	a	a	a	a	a	a	a
886	107	5.9	4.1	1.8	2.3	41	14	10.7	9.8
887	102	5.8	3.8	2.0	1.9	37	10	10.1	9.5
888	105	5.7	3.8	1.9	2.0	40	16	10.4	9.1
889	112	5.4	3.7	1.7	2.2	36	9	10.4	11.1
890	108	5.7	3.8	1.9	2.0	42	16	10.6	9.7
MEAN	107	5.7	3.8	1.9	2.1	39	13	10.4	9.8
SD	3.7	0.19	0.15	0.11	0.16	2.6	3.3	0.23	0.75
N	5	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (μmol/L)

Fasted Males

Animal ID	Day 15	Day 29
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
806	20.4	a
807	21.4	a
808	26.6	a
809	24.9	a
810	17.3	a
811	NA	19.2
812	NA	19.8
813	NA	21.2
814	NA	18.5
815	NA	27.0
MEAN	22.1	21.1
SD	3.69	3.42
N	5	5

Non-Fasted Males

Animal ID	Day 15	Day 29
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
806	NA	NA
807	NA	NA
808	NA	NA
809	NA	NA
810	NA	NA
811	10.9	NA
812	13.9	NA
813	10.4	NA
814	10.9	NA
815	14.2	NA
MEAN	12.1	NA
SD	1.83	NA
N	5	0

a – Sacrificed day 15
NA – not applicable

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (µmol/L)

Fasted Males

Animal ID	Day 15	Day 29
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM		
836	19.2	a
837	18.0	a
838	19.3	a
839	16.4	a
840	18.3	a
841	NA	27.3
842	NA	17.1
843	NA	21.6
844	NA	22.5
845	NA	15.5
MEAN	18.2	20.8
SD	1.17	4.68
N	5	5

Non-Fasted Males

Animal ID	Day 15	Day 29
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM		
836	NA	NA
837	NA	NA
838	NA	NA
839	NA	NA
840	NA	NA
841	9.2	NA
842	15.1	NA
843	12.0	NA
844	9.1	NA
845	15.1	NA
MEAN	12.1	NA
SD	2.98	NA
N	5	0

a – Sacrificed day 15
NA – not applicable

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (μmol/L)

Fasted Males

Animal ID	Day 15	Day 29
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM		
866	21.3	a
867	23.8	a
868	17.0	a
869	22.5	a
870	14.8	a
871	NA	16.7
872	NA	18.5
873	NA	35.4
874	NA	16.1
875	NA	16.9
MEAN	19.9	20.7
SD	3.82	8.25
N	5	5

Non-Fasted Males

Animal ID	Day 15	Day 29
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM		
866	NA	NA
867	NA	NA
868	NA	NA
869	NA	NA
870	NA	NA
871	24.8	NA
872	12.7	NA
873	14.5	NA
874	8.0	NA
875	10.9	NA
MEAN	14.2	NA
SD	6.40	NA
N	5	0

a – Sacrificed day 15
NA – not applicable

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (μmol/L)

Fasted Females

Animal ID	Day 15	Day 29
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
821	16.2	a
822	20.4	a
823	24.0	a
824	17.3	a
825	14.8	a
826	NA	22.7
827	NA	16.3
828	NA	22.6
829	NA	14.5
830	NA	32.8
MEAN	18.5	21.8
SD	3.68	7.18
N	5	5

Non-Fasted Females

Animal ID	Day 15	Day 29
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)		
821	NA	NA
822	NA	NA
823	NA	NA
824	NA	NA
825	NA	NA
826	22.9	NA
827	5.4	NA
828	10.7	NA
829	32.8	NA
830	37.4	NA
MEAN	21.8	NA
SD	13.76	NA
N	5	0

a – Sacrificed day 15
NA – not applicable

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (μmol/L)

Fasted Females

Animal ID	Day 15	Day 29
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM		
851	23.4	a
852	13.7	a
853	14.3	a
854	17.7	a
855	18.7	a
856	NA	24.3
857	NA	24.6
858	NA	16.5
859	NA	15.9
860	NA	22.7
MEAN	17.6	20.8
SD	3.90	4.27
N	5	5

Non-Fasted Females

Animal ID	Day 15	Day 29
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM		
851	NA	NA
852	NA	NA
853	NA	NA
854	NA	NA
855	NA	NA
856	9.1	NA
857	19.7	NA
858	7.5	NA
859	11.6	NA
860	5.8	NA
MEAN	10.7	NA
SD	5.45	NA
N	5	0

a – Sacrificed day 15
NA – not applicable

Appendix C Table C-7 (cont.)

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
TEST: Total Bile Acid (μmol/L)

Fasted Females

Animal ID	Day 15	Day 29
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM		
881	17.1	a
882	15.2	a
883	16.6	a
884	16.9	a
885	17.3	a
886	NA	21.1
887	NA	14.8
888	NA	35.1
889	NA	43.8
890	NA	25.1
MEAN	16.6	28.0
SD	0.83	11.51
N	5	5

Non-Fasted Females

Animal ID	Day 15	Day 29
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM		
881	NA	NA
882	NA	NA
883	NA	NA
884	NA	NA
885	NA	NA
886	18.0	NA
887	12.3	NA
888	9.0	NA
889	8.8	NA
890	39.6	NA
MEAN	17.5	NA
SD	12.88	NA
N	5	0

a – Sacrificed day 15
NA – not applicable

Appendix C Table C-8

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
806	12.69	8.63	15.3	49.5	57.4	17.7	30.8	768
807	12.86	8.43	15.2	47.6	56.4	18.0	31.9	773
808	11.23	8.60	15.6	48.9	56.8	18.2	32.0	858
809	11.12	8.54	15.1	49.3	57.7	17.7	30.7	818
810	13.44	8.34	14.9	47.3	56.6	17.8	31.5	783
811	11.98	8.58	15.3	47.5	55.4	17.8	32.2	840
812	12.17	8.37	15.5	47.7	57.0	18.5	32.5	873
813	11.06	8.06	15.2	45.0	55.8	18.8	33.8	891
814	12.18	8.40	15.2	47.8	57.0	18.1	31.7	819
815	12.84	8.55	15.1	48.0	56.2	17.7	31.5	847
MEAN	12.16	8.45	15.2	47.9	56.6	18.0	31.9	827
SD	0.821	0.171	0.20	1.27	0.71	0.38	0.89	42.5
N	10	10	10	10	10	10	10	10
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
836	11.65	8.22	14.8	47.0	57.2	18.0	31.5	827
837	11.74	8.83	15.6	50.1	56.7	17.7	31.1	701
838	11.48	8.57	15.4	47.6	55.5	17.9	32.3	775
839	11.36	9.03	15.9	50.7	56.2	17.6	31.4	675
840	11.64	8.86	15.6	49.2	55.6	17.6	31.7	863
841	11.23	8.95	15.7	50.3	56.2	17.5	31.2	915
842	13.68	8.77	15.7	49.5	56.5	17.9	31.7	598
843	12.17	8.87	15.7	50.8	57.3	17.7	31.0	853
844	11.67	8.40	15.1	46.2	55.0	18.0	32.8	834
845	12.15	8.41	14.9	47.1	56.0	17.7	31.6	837
MEAN	11.88	8.69	15.4	48.8	56.2	17.8	31.6	788
SD	0.701	0.272	0.38	1.72	0.74	0.18	0.55	99.2
N	10	10	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
806	3.0	257.8	20.8	75.1	2.7	0.3	0.8	0.3
807	3.5	295.7	16.2	80.2	2.1	0.7	0.6	0.3
808	2.8	243.0	13.0	84.1	1.8	0.3	0.4	0.3
809	2.8	240.0	15.6	81.6	1.6	0.4	0.7	0.2
810	3.1	255.8	19.6	77.5	1.7	0.4	0.7	0.1
811	2.4	206.4	15.9	80.1	2.7	0.7	0.4	0.2
812	2.9	245.0	19.2	78.1	1.4	0.6	0.5	0.1
813	3.3	266.0	15.2	80.2	3.1	0.6	0.6	0.3
814	3.3	276.6	13.9	81.9	2.6	0.7	0.5	0.4
815	3.2	269.4	18.1	77.8	2.7	0.6	0.5	0.3
MEAN	3.0	255.6	16.8	79.7	2.2	0.5	0.6	0.3
SD	0.32	24.24	2.57	2.60	0.59	0.16	0.13	0.10
N	10	10	10	10	10	10	10	10
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
836	2.8	232.3	14.8	80.7	3.1	0.3	0.6	0.5
837	2.1	181.5	20.2	76.0	2.4	0.5	0.6	0.3
838	2.7	230.6	18.5	77.1	2.9	0.5	0.6	0.4
839	2.8	248.7	12.9	83.7	1.9	0.7	0.5	0.3
840	2.7	234.9	14.2	82.3	2.2	0.6	0.4	0.4
841	2.8	253.2	16.6	79.3	2.6	0.5	0.7	0.3
842	2.7	235.4	19.2	76.3	2.9	0.8	0.5	0.4
843	2.7	241.0	15.2	81.2	2.3	0.3	0.7	0.2
844	2.7	224.5	17.0	77.9	3.4	0.8	0.4	0.5
845	3.0	249.7	17.8	78.6	2.2	0.6	0.5	0.3
MEAN	2.7	233.2	16.6	79.3	2.6	0.6	0.6	0.4
SD	0.23	20.38	2.35	2.61	0.47	0.18	0.11	0.10
N	10	10	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
806	2.64	9.52	0.34	0.04	0.10	0.03
807	2.08	10.31	0.27	0.10	0.07	0.04
808	1.46	9.45	0.21	0.04	0.05	0.03
809	1.73	9.07	0.17	0.05	0.07	0.03
810	2.63	10.41	0.23	0.06	0.10	0.02
811	1.90	9.60	0.32	0.09	0.04	0.03
812	2.34	9.51	0.17	0.07	0.06	0.02
813	1.68	8.88	0.34	0.07	0.06	0.03
814	1.69	9.98	0.32	0.09	0.06	0.04
815	2.32	9.99	0.35	0.07	0.07	0.03
MEAN	2.05	9.67	0.27	0.07	0.07	0.03
SD	0.419	0.499	0.072	0.021	0.019	0.007
N	10	10	10	10	10	10
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM						
836	1.73	9.40	0.36	0.04	0.07	0.05
837	2.37	8.93	0.28	0.06	0.07	0.03
838	2.12	8.85	0.33	0.05	0.07	0.04
839	1.46	9.51	0.22	0.08	0.06	0.03
840	1.65	9.58	0.26	0.06	0.04	0.04
841	1.87	8.90	0.29	0.06	0.08	0.03
842	2.63	10.43	0.39	0.10	0.07	0.05
843	1.84	9.88	0.29	0.04	0.09	0.03
844	1.99	9.10	0.40	0.10	0.04	0.05
845	2.16	9.55	0.27	0.07	0.07	0.03
MEAN	1.98	9.41	0.31	0.07	0.07	0.04
SD	0.350	0.497	0.059	0.022	0.016	0.009
N	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
866	12.90	8.92	15.3	50.4	56.5	17.2	30.4	807
867	12.05	8.67	15.7	48.9	56.4	18.1	32.0	816
868	12.45	8.73	15.6	50.2	57.5	17.9	31.1	805
869	11.32	8.87	15.8	49.5	55.8	17.8	32.0	883
870	11.37	8.31	14.9	47.0	56.5	17.9	31.7	813
871	12.92	8.92	15.6	50.5	56.6	17.4	30.8	902
872	12.80	8.78	15.6	48.5	55.2	17.7	32.1	878
873	13.32	8.52	15.3	47.2	55.4	17.9	32.4	812
874	12.13	8.48	15.3	47.8	56.4	18.1	32.1	762
875	12.41	8.79	15.3	48.7	55.4	17.4	31.4	807
MEAN	12.37	8.70	15.4	48.9	56.2	17.7	31.6	829
SD	0.662	0.204	0.27	1.28	0.71	0.31	0.65	44.0
N	10	10	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
866	2.5	221.5	18.1	77.6	2.8	0.4	0.6	0.4
867	2.9	247.8	14.2	81.7	2.7	0.4	0.7	0.3
868	2.6	225.1	14.8	80.3	1.9	1.7	1.1	0.3
869	3.3	288.4	15.2	80.9	2.2	0.9	0.5	0.4
870	2.9	241.8	13.5	83.7	1.5	0.5	0.4	0.4
871	2.8	252.6	13.6	82.4	2.5	0.6	0.7	0.2
872	2.6	227.9	12.9	84.1	1.6	0.6	0.5	0.4
873	2.6	224.2	14.9	81.5	2.2	0.5	0.6	0.3
874	2.4	205.9	15.1	80.4	2.7	0.6	0.7	0.4
875	2.6	229.6	21.5	73.6	3.1	0.9	0.5	0.4
MEAN	2.7	236.5	15.4	80.6	2.3	0.7	0.6	0.4
SD	0.26	22.79	2.58	3.08	0.53	0.39	0.19	0.07
N	10	10	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM						
866	2.34	10.01	0.36	0.05	0.08	0.05
867	1.71	9.84	0.33	0.05	0.08	0.04
868	1.84	9.99	0.24	0.21	0.14	0.03
869	1.72	9.16	0.25	0.10	0.05	0.04
870	1.53	9.51	0.18	0.05	0.05	0.05
871	1.76	10.64	0.33	0.07	0.09	0.03
872	1.65	10.77	0.20	0.07	0.06	0.05
873	1.99	10.85	0.29	0.07	0.07	0.04
874	1.84	9.75	0.33	0.07	0.09	0.05
875	2.67	9.13	0.39	0.11	0.06	0.04
MEAN	1.91	9.97	0.29	0.09	0.08	0.04
SD	0.348	0.624	0.070	0.048	0.027	0.008
N	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
821	12.12	8.95	16.0	48.9	54.6	17.9	32.7	708
822	10.63	8.29	15.1	46.0	55.5	18.3	32.9	904
823	10.46	8.08	14.6	45.3	56.1	18.1	32.2	838
824	11.37	8.39	15.5	46.6	55.5	18.4	33.2	840
825	12.41	8.38	15.4	47.7	56.9	18.4	32.3	746
826	11.36	8.05	14.7	46.4	57.7	18.2	31.6	970
827	11.87	8.57	15.6	48.0	56.0	18.2	32.5	753
828	11.72	8.09	14.8	45.9	56.8	18.3	32.2	834
829	11.90	8.40	14.9	47.1	56.0	17.8	31.7	761
830	10.37	8.32	15.1	46.8	56.3	18.2	32.3	701
MEAN	11.42	8.35	15.2	46.9	56.1	18.2	32.4	806
SD	0.719	0.268	0.45	1.09	0.86	0.20	0.49	87.3
N	10	10	10	10	10	10	10	10
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
851	10.27	7.55	13.6	42.1	55.8	18.0	32.3	790
852	10.33	8.49	15.8	47.0	55.4	18.6	33.5	751
853	10.31	8.50	15.2	46.6	54.9	17.9	32.6	654
854	10.64	7.67	13.6	42.6	55.5	17.7	31.9	779
855	10.94	8.82	16.2	49.8	56.5	18.3	32.5	798
856	11.82	7.84	14.5	44.2	56.4	18.5	32.7	868
857	12.03	8.68	15.9	48.4	55.8	18.3	32.9	631
858	10.70	7.65	14.7	44.2	57.7	19.2	33.3	589
859	11.58	8.35	15.5	47.6	57.0	18.5	32.5	797
860	11.34	8.33	15.3	47.1	56.5	18.3	32.4	790
MEAN	11.00	8.19	15.0	46.0	56.2	18.3	32.7	745
SD	0.655	0.467	0.91	2.55	0.83	0.42	0.47	89.1
N	10	10	10	10	10	10	10	10

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
821	1.9	168.0	9.6	86.4	2.2	0.7	0.6	0.5
822	2.0	168.9	15.6	80.3	2.6	0.4	0.7	0.4
823	2.5	197.9	19.6	76.4	2.7	0.4	0.6	0.3
824	1.9	156.2	16.7	78.7	2.5	1.0	0.7	0.5
825	2.5	208.6	11.6	84.7	2.0	0.6	0.7	0.4
826	2.7	215.6	15.4	79.2	3.6	0.6	0.8	0.4
827	1.8	156.7	19.4	75.9	2.6	0.9	0.8	0.4
828	2.0	161.9	15.3	80.7	2.3	0.6	0.8	0.3
829	2.6	215.7	14.7	80.0	3.5	0.5	0.8	0.4
830	2.0	163.5	15.8	79.1	3.3	0.5	0.9	0.4
MEAN	2.2	181.3	15.4	80.1	2.7	0.6	0.7	0.4
SD	0.34	25.03	3.06	3.27	0.55	0.20	0.10	0.07
N	10	10	10	10	10	10	10	10
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
851	2.1	159.2	17.9	77.8	2.4	0.5	0.9	0.4
852	2.3	191.6	13.9	81.2	3.1	1.1	0.5	0.2
853	2.0	173.3	15.9	79.3	2.7	0.8	0.7	0.4
854	2.4	184.3	15.5	80.0	2.8	0.6	0.7	0.5
855	2.1	184.1	15.9	80.1	2.5	0.5	0.7	0.3
856	2.6	207.0	25.3	71.7	1.5	0.5	0.6	0.4
857	2.1	183.0	24.3	72.1	2.2	0.6	0.5	0.3
858	2.6	198.6	14.3	82.5	1.5	0.6	1.0	0.1
859	2.5	206.1	14.6	80.5	2.9	0.7	0.9	0.4
860	2.4	203.8	14.9	80.0	3.4	0.6	0.8	0.2
MEAN	2.3	189.1	17.3	78.5	2.5	0.7	0.7	0.3
SD	0.22	15.46	4.14	3.69	0.63	0.18	0.17	0.12
N	10	10	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
821	1.17	10.47	0.26	0.09	0.07	0.06
822	1.66	8.53	0.28	0.05	0.07	0.04
823	2.05	7.99	0.28	0.04	0.07	0.03
824	1.90	8.94	0.28	0.11	0.08	0.06
825	1.44	10.50	0.25	0.08	0.08	0.04
826	1.75	9.00	0.40	0.06	0.09	0.05
827	2.30	9.01	0.31	0.11	0.09	0.05
828	1.80	9.47	0.27	0.07	0.09	0.04
829	1.75	9.52	0.42	0.06	0.09	0.05
830	1.64	8.20	0.35	0.05	0.09	0.04
MEAN	1.75	9.16	0.31	0.07	0.08	0.05
SD	0.311	0.851	0.060	0.025	0.009	0.010
N	10	10	10	10	10	10
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM						
851	1.84	7.99	0.25	0.06	0.09	0.04
852	1.44	8.39	0.32	0.11	0.05	0.02
853	1.64	8.18	0.28	0.09	0.07	0.05
854	1.65	8.51	0.30	0.06	0.07	0.05
855	1.74	8.76	0.28	0.06	0.08	0.03
856	2.99	8.47	0.18	0.05	0.07	0.05
857	2.92	8.68	0.27	0.07	0.06	0.04
858	1.53	8.83	0.16	0.06	0.11	0.01
859	1.69	9.32	0.34	0.08	0.10	0.05
860	1.69	9.07	0.39	0.07	0.09	0.03
MEAN	1.91	8.62	0.28	0.07	0.08	0.04
SD	0.560	0.400	0.069	0.018	0.019	0.014
N	10	10	10	10	10	10

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
881	13.19	8.30	15.5	45.7	55.1	18.7	33.9	671
882	12.28	8.35	15.0	46.9	56.1	18.0	32.1	677
883	10.59	8.31	15.3	46.2	55.6	18.4	33.2	805
884	13.51	8.45	15.3	46.8	55.4	18.1	32.7	805
885	11.79	8.35	15.5	47.0	56.3	18.5	32.9	688
886	10.44	8.42	15.4	46.6	55.3	18.3	33.1	772
887	9.70	8.30	15.4	47.3	57.0	18.5	32.5	687
888	10.59	7.90	14.6	44.6	56.5	18.5	32.8	692
889	10.41	8.90	15.8	50.7	56.9	17.8	31.3	753
890	12.69	8.36	14.9	46.8	56.0	17.8	31.8	747
MEAN	11.52	8.36	15.3	46.9	56.0	18.3	32.6	730
SD	1.342	0.241	0.35	1.56	0.66	0.32	0.75	52.9
N	10	10	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
881	2.1	176.8	13.6	82.8	2.0	0.8	0.5	0.3
882	2.1	174.5	13.3	82.8	2.4	0.7	0.6	0.3
883	2.7	228.4	19.6	76.8	1.9	0.9	0.5	0.3
884	2.0	167.3	20.7	75.8	1.9	0.6	0.6	0.4
885	2.3	189.3	13.1	82.3	2.9	0.8	0.6	0.3
886	2.2	185.4	15.2	79.7	2.8	1.3	0.6	0.4
887	2.0	168.1	15.2	79.4	3.6	0.7	0.7	0.3
888	2.1	163.1	20.0	74.8	3.3	0.8	0.8	0.3
889	1.9	170.8	12.0	84.1	1.9	0.8	1.0	0.3
890	2.3	196.4	17.1	77.2	3.7	0.7	0.8	0.5
MEAN	2.2	182.0	16.0	79.6	2.6	0.8	0.7	0.3
SD	0.23	19.44	3.18	3.32	0.72	0.19	0.16	0.07
N	10	10	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 8

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM						
881	1.79	10.93	0.26	0.10	0.07	0.04
882	1.63	10.17	0.29	0.09	0.07	0.03
883	2.07	8.13	0.20	0.10	0.05	0.04
884	2.80	10.25	0.26	0.08	0.08	0.05
885	1.55	9.70	0.34	0.09	0.07	0.04
886	1.59	8.33	0.29	0.14	0.06	0.04
887	1.47	7.71	0.35	0.07	0.07	0.03
888	2.12	7.92	0.35	0.09	0.08	0.04
889	1.25	8.75	0.20	0.08	0.10	0.03
890	2.17	9.80	0.47	0.09	0.10	0.06
MEAN	1.84	9.17	0.30	0.09	0.08	0.04
SD	0.452	1.135	0.081	0.019	0.016	0.009
N	10	10	10	10	10	10

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
806	9.35	8.50	15.0	47.9	56.4	17.6	31.3	849
807	9.35	8.06	14.5	46.7	58.0	18.0	31.0	902
808	10.82	8.49	15.0	48.7	57.4	17.6	30.7	866
809	9.69	8.06	14.6	46.4	57.6	18.1	31.4	926
810	9.52	8.12	14.2	45.3	55.8	17.5	31.3	838
MEAN	9.75	8.25	14.7	47.0	57.0	17.8	31.1	876
SD	0.617	0.229	0.34	1.33	0.91	0.27	0.29	36.9
N	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
811	9.84	8.10	14.2	46.1	56.9	17.5	30.7	980
812	12.18	8.26	14.5	47.2	57.2	17.5	30.6	959
813	9.70	7.65	13.7	43.6	57.0	17.9	31.5	823
814	11.47	8.46	14.9	48.6	57.5	17.7	30.8	860
815	10.70	8.64	15.2	49.8	57.6	17.6	30.5	907
MEAN	10.78	8.22	14.5	47.1	57.2	17.6	30.8	906
SD	1.060	0.379	0.59	2.39	0.30	0.17	0.40	65.7
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
806	4.2	352.7	17.1	80.2	1.3	0.6	0.5	0.2
807	4.9	394.9	16.8	80.1	1.7	0.8	0.4	0.3
808	4.7	400.2	20.2	76.8	1.4	0.7	0.6	0.3
809	5.0	399.2	25.3	71.5	2.0	0.5	0.4	0.2
810	4.4	354.1	20.6	75.8	1.2	1.8	0.4	0.2
MEAN	4.6	380.2	20.0	76.9	1.5	0.9	0.5	0.2
SD	0.34	24.57	3.43	3.59	0.33	0.53	0.09	0.05
N	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
811	5.1	412.9	19.3	77.1	2.2	0.6	0.4	0.5
812	5.5	455.8	19.9	76.1	3.0	0.5	0.4	0.1
813	4.6	349.4	15.2	80.5	3.2	0.5	0.4	0.3
814	4.8	406.4	17.0	77.6	3.7	0.7	0.5	0.4
815	4.8	418.8	16.5	79.6	2.8	0.5	0.4	0.3
MEAN	5.0	408.7	17.6	78.2	3.0	0.6	0.4	0.3
SD	0.35	38.27	1.97	1.82	0.55	0.09	0.04	0.15
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
806	1.60	7.50	0.12	0.06	0.04	0.02
807	1.57	7.48	0.16	0.07	0.04	0.03
808	2.19	8.31	0.15	0.08	0.06	0.03
809	2.45	6.93	0.20	0.05	0.04	0.02
810	1.96	7.22	0.12	0.17	0.04	0.02
MEAN	1.95	7.49	0.15	0.09	0.04	0.02
SD	0.379	0.515	0.033	0.048	0.009	0.005
N	5	5	5	5	5	5

Non-Fasted Males

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
811	1.90	7.59	0.22	0.06	0.04	0.05
812	2.43	9.27	0.36	0.06	0.05	0.02
813	1.47	7.80	0.31	0.05	0.04	0.03
814	1.95	8.90	0.43	0.08	0.06	0.05
815	1.76	8.51	0.30	0.05	0.04	0.03
MEAN	1.90	8.41	0.32	0.06	0.05	0.04
SD	0.349	0.713	0.078	0.012	0.009	0.013
N	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
836	9.69	8.33	14.9	46.9	56.2	17.8	31.7	892
837	10.64	8.65	15.2	47.9	55.4	17.6	31.7	874
838	11.02	8.58	15.0	47.8	55.7	17.5	31.4	921
839	10.75	8.63	15.2	48.0	55.6	17.6	31.7	957
840	10.82	8.64	15.2	47.7	55.2	17.6	32.0	856
MEAN	10.58	8.57	15.1	47.7	55.6	17.6	31.7	900
SD	0.519	0.135	0.14	0.44	0.38	0.11	0.21	39.9
N	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
841	10.02	8.07	14.5	46.4	57.5	18.0	31.3	853
842	11.76	7.90	14.5	45.7	57.8	18.4	31.8	869
843	11.15	8.72	15.4	50.1	57.5	17.6	30.7	908
844	10.23	8.35	14.6	47.7	57.1	17.5	30.6	864
845	11.16	8.28	14.4	47.5	57.4	17.4	30.3	901
MEAN	10.86	8.26	14.7	47.5	57.5	17.8	30.9	879
SD	0.722	0.311	0.41	1.68	0.25	0.41	0.60	24.1
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
836	4.6	382.5	19.3	76.8	2.1	1.0	0.4	0.3
837	4.1	354.6	19.5	75.9	2.7	1.2	0.3	0.3
838	4.5	382.9	21.4	74.0	2.9	0.9	0.4	0.4
839	4.8	413.5	21.0	75.6	1.8	0.9	0.4	0.2
840	4.0	345.0	21.6	74.3	1.9	1.4	0.4	0.4
MEAN	4.4	375.7	20.6	75.3	2.3	1.1	0.4	0.3
SD	0.34	26.99	1.08	1.16	0.49	0.22	0.04	0.08
N	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
841	4.7	378.4	16.5	79.5	2.8	0.4	0.5	0.3
842	4.7	373.5	19.4	77.0	2.5	0.3	0.5	0.2
843	4.9	424.7	16.2	80.0	2.3	0.6	0.3	0.5
844	4.6	382.0	21.4	75.0	2.8	0.4	0.3	0.3
845	4.6	382.8	18.0	78.0	2.8	0.5	0.4	0.3
MEAN	4.7	388.3	18.3	77.9	2.6	0.4	0.4	0.3
SD	0.12	20.69	2.15	2.01	0.23	0.11	0.10	0.11
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM						
836	1.87	7.44	0.21	0.10	0.03	0.03
837	2.08	8.08	0.29	0.13	0.03	0.03
838	2.36	8.16	0.32	0.10	0.04	0.04
839	2.26	8.13	0.20	0.10	0.04	0.02
840	2.34	8.04	0.20	0.15	0.05	0.04
MEAN	2.18	7.97	0.24	0.12	0.04	0.03
SD	0.206	0.300	0.057	0.023	0.008	0.008
N	5	5	5	5	5	5

Non-Fasted Males

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 2-M:0.075 mg/kg/day CuATSM / H2ATSM						
841	1.66	7.97	0.28	0.04	0.05	0.03
842	2.28	9.06	0.29	0.03	0.06	0.03
843	1.81	8.93	0.26	0.07	0.04	0.06
844	2.19	7.67	0.28	0.04	0.03	0.03
845	2.01	8.70	0.31	0.06	0.04	0.04
MEAN	1.99	8.47	0.28	0.05	0.04	0.04
SD	0.258	0.613	0.018	0.016	0.011	0.013
N	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
866	12.08	8.47	14.6	46.5	55.0	17.2	31.3	916
867	10.58	8.52	15.2	48.7	57.2	17.9	31.3	870
868	11.89	8.81	15.3	49.8	56.5	17.4	30.8	691
869	9.34	8.40	15.0	48.1	57.2	17.8	31.1	820
870	10.44	8.43	14.9	48.6	57.7	17.7	30.7	915
MEAN	10.87	8.53	15.0	48.3	56.7	17.6	31.0	842
SD	1.131	0.165	0.27	1.20	1.05	0.29	0.28	93.4
N	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
871	13.84	8.65	15.1	50.1	58.0	17.4	30.1	908
872	11.21	7.97	14.2	45.4	57.0	17.8	31.3	876
873	10.17	8.53	14.7	48.3	56.6	17.2	30.4	846
874	11.38	8.72	15.3	50.3	57.7	17.6	30.5	903
875	10.94	8.36	14.3	48.3	57.7	17.1	29.6	868
MEAN	11.51	8.45	14.7	48.5	57.4	17.4	30.4	880
SD	1.383	0.299	0.48	1.97	0.58	0.29	0.62	25.6
N	5	5	5	5	5	5	5	5

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
866	4.8	404.2	17.7	77.4	2.7	0.9	0.7	0.5
867	4.0	340.3	17.0	80.0	1.7	0.8	0.4	0.2
868	3.8	333.7	17.0	78.8	2.7	0.7	0.5	0.4
869	4.8	399.3	20.1	75.9	2.7	0.7	0.3	0.3
870	5.0	417.8	17.5	79.4	1.8	0.5	0.4	0.3
MEAN	4.5	379.1	17.9	78.3	2.3	0.7	0.5	0.3
SD	0.54	39.06	1.29	1.65	0.52	0.15	0.15	0.11
N	5	5	5	5	5	5	5	5

Non-Fasted Males

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
871	6.5	563.7	19.3	76.5	2.9	0.7	0.4	0.1
872	4.2	336.6	14.5	82.0	2.1	0.7	0.3	0.4
873	4.1	352.9	15.1	81.3	2.1	0.7	0.5	0.3
874	4.8	414.8	16.4	80.3	2.2	0.5	0.4	0.2
875	4.5	372.3	16.5	80.2	2.2	0.4	0.4	0.2
MEAN	4.8	408.1	16.4	80.1	2.3	0.6	0.4	0.2
SD	0.98	91.78	1.85	2.12	0.34	0.14	0.07	0.11
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Males

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM						
866	2.14	9.35	0.33	0.11	0.08	0.06
867	1.80	8.46	0.18	0.08	0.04	0.02
868	2.02	9.36	0.32	0.08	0.07	0.05
869	1.87	7.08	0.26	0.06	0.03	0.03
870	1.83	8.28	0.19	0.06	0.04	0.03
MEAN	1.93	8.51	0.26	0.08	0.05	0.04
SD	0.144	0.939	0.070	0.020	0.022	0.016
N	5	5	5	5	5	5

Non-Fasted Males

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 3-M:0.150 mg/kg/day CuATSM / H2ATSM						
871	2.68	10.60	0.40	0.09	0.06	0.02
872	1.63	9.19	0.23	0.07	0.04	0.05
873	1.54	8.27	0.21	0.07	0.05	0.03
874	1.87	9.14	0.25	0.05	0.05	0.02
875	1.81	8.78	0.24	0.05	0.04	0.03
MEAN	1.91	9.20	0.27	0.07	0.05	0.03
SD	0.453	0.867	0.076	0.017	0.008	0.012
N	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
821	10.40	7.99	14.2	45.4	56.8	17.8	31.4	812
822	8.65	7.70	14.3	44.8	58.2	18.6	31.9	940
823	9.36	7.85	15.0	46.0	58.6	19.1	32.6	807
824	5.67	6.84	12.7	38.4	56.2	18.6	33.1	856
825	9.61	8.01	15.0	46.8	58.4	18.7	32.1	858
MEAN	8.74	7.68	14.2	44.3	57.6	18.6	32.2	855
SD	1.826	0.485	0.94	3.37	1.07	0.47	0.65	53.4
N	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
826	9.00	7.56	13.9	45.3	60.0	18.4	30.7	1038
827	9.55	6.94	12.7	40.6	58.5	18.2	31.2	712
828	9.80	7.73	14.3	47.0	60.8	18.6	30.5	942
829	9.67	7.70	14.3	46.0	59.7	18.5	31.0	1079
830	10.29	7.77	14.2	44.8	57.6	18.2	31.6	980
MEAN	9.66	7.54	13.9	44.7	59.3	18.4	31.0	950
SD	0.465	0.345	0.68	2.46	1.27	0.18	0.43	143.2
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
821	5.3	425.9	18.1	78.8	1.8	0.6	0.4	0.4
822	5.0	383.3	17.9	79.8	1.3	0.5	0.4	0.2
823	4.4	344.3	17.2	80.1	1.5	0.6	0.3	0.3
824	6.3	431.5	37.8	58.0	3.0	0.7	0.2	0.1
825	5.4	435.0	15.7	81.3	1.5	0.7	0.5	0.3
MEAN	5.3	404.0	21.3	75.6	1.8	0.6	0.4	0.3
SD	0.69	39.34	9.25	9.88	0.68	0.08	0.11	0.11
N	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
826	4.2	316.9	18.3	78.9	1.5	0.6	0.5	0.2
827	5.1	355.3	17.8	78.3	1.9	0.6	0.7	0.8
828	6.0	462.3	15.4	81.8	1.4	0.7	0.4	0.2
829	5.5	423.2	15.2	80.9	2.8	0.3	0.5	0.4
830	5.5	425.9	12.7	84.8	1.5	0.5	0.3	0.2
MEAN	5.3	396.7	15.9	80.9	1.8	0.5	0.5	0.4
SD	0.67	59.03	2.26	2.59	0.58	0.15	0.15	0.26
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
821	1.88	8.19	0.18	0.06	0.04	0.04
822	1.55	6.90	0.11	0.04	0.04	0.01
823	1.61	7.50	0.14	0.06	0.03	0.03
824	2.14	3.29	0.17	0.04	0.01	0.01
825	1.51	7.81	0.14	0.07	0.05	0.03
MEAN	1.74	6.74	0.15	0.05	0.03	0.02
SD	0.267	1.985	0.028	0.013	0.015	0.013
N	5	5	5	5	5	5

Non-Fasted Females

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
826	1.64	7.10	0.14	0.05	0.04	0.02
827	1.70	7.48	0.18	0.06	0.06	0.08
828	1.51	8.02	0.14	0.07	0.04	0.02
829	1.47	7.82	0.27	0.03	0.05	0.03
830	1.31	8.72	0.15	0.05	0.04	0.02
MEAN	1.53	7.83	0.18	0.05	0.05	0.03
SD	0.153	0.609	0.055	0.015	0.009	0.026
N	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
851	11.94	7.58	14.2	45.1	59.5	18.7	31.5	929
852	10.23	8.10	14.8	46.1	56.9	18.3	32.1	1003
853	11.66	8.07	14.8	46.8	58.0	18.3	31.6	841
854	10.78	7.94	14.6	47.5	59.8	18.3	30.7	1065
855	8.21	8.48	15.5	48.9	57.7	18.3	31.7	817
MEAN	10.56	8.03	14.8	46.9	58.4	18.4	31.5	931
SD	1.483	0.324	0.47	1.44	1.23	0.18	0.51	105.2
N	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
856	9.10	7.95	14.6	46.8	58.9	18.4	31.3	889
857	9.35	7.48	14.4	43.5	58.1	19.2	33.0	981
858	9.92	7.93	14.5	47.4	59.7	18.3	30.6	724
859	9.28	7.74	14.4	45.3	58.5	18.6	31.8	858
860	11.22	7.98	14.5	46.9	58.7	18.2	31.0	970
MEAN	9.77	7.82	14.5	46.0	58.8	18.5	31.5	884
SD	0.865	0.210	0.08	1.59	0.59	0.40	0.93	103.8
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
851	6.2	469.5	17.3	80.4	1.0	0.6	0.5	0.3
852	5.1	414.0	17.2	78.5	2.7	0.8	0.4	0.4
853	4.9	396.0	19.3	76.4	2.4	0.9	0.4	0.5
854	7.5	599.2	21.0	76.0	1.6	0.8	0.3	0.4
855	5.2	443.4	18.3	77.8	2.1	1.0	0.6	0.3
MEAN	5.8	464.4	18.6	77.8	2.0	0.8	0.4	0.4
SD	1.08	80.40	1.58	1.76	0.67	0.15	0.11	0.08
N	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
856	4.4	347.4	15.3	82.2	1.4	0.8	0.3	0.1
857	5.2	387.4	16.1	79.8	2.7	0.6	0.4	0.4
858	4.1	328.2	11.9	85.4	1.3	0.6	0.4	0.3
859	4.8	374.3	17.6	77.8	2.9	0.8	0.6	0.3
860	4.7	377.6	16.1	81.3	1.4	0.6	0.4	0.2
MEAN	4.6	363.0	15.4	81.3	1.9	0.7	0.4	0.3
SD	0.42	24.45	2.13	2.83	0.79	0.11	0.11	0.11
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM						
851	2.07	9.59	0.12	0.07	0.05	0.03
852	1.76	8.03	0.28	0.08	0.04	0.04
853	2.25	8.91	0.28	0.11	0.05	0.05
854	2.27	8.19	0.17	0.08	0.03	0.04
855	1.50	6.38	0.17	0.08	0.05	0.02
MEAN	1.97	8.22	0.20	0.08	0.04	0.04
SD	0.333	1.202	0.072	0.015	0.009	0.011
N	5	5	5	5	5	5

Non-Fasted Females

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 2-F:0.075 mg/kg/day CuATSM / H2ATSM						
856	1.39	7.48	0.13	0.07	0.02	0.01
857	1.51	7.47	0.25	0.06	0.03	0.04
858	1.18	8.48	0.13	0.06	0.04	0.03
859	1.64	7.22	0.27	0.08	0.05	0.03
860	1.80	9.13	0.16	0.07	0.05	0.02
MEAN	1.50	7.96	0.19	0.07	0.04	0.03
SD	0.237	0.815	0.067	0.008	0.013	0.011
N	5	5	5	5	5	5

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
881	10.40	8.19	14.9	47.6	58.1	18.3	31.4	762
882	10.89	7.98	14.5	45.9	57.6	18.2	31.6	961
883	9.47	7.69	14.6	46.5	60.5	19.0	31.5	1079
884	9.87	8.07	15.0	48.1	59.6	18.6	31.2	946
885	9.42	8.19	14.8	45.8	56.0	18.1	32.4	1003
MEAN	10.01	8.02	14.8	46.8	58.4	18.4	31.6	950
SD	0.630	0.207	0.21	1.03	1.76	0.36	0.46	117.2
N	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
886	8.98	7.65	14.1	45.6	59.7	18.4	30.9	902
887	10.25	6.78	12.6	40.8	60.1	18.6	31.0	1159
888	8.09	7.35	13.8	43.0	58.5	18.7	32.0	829
889	11.11	8.14	14.5	47.3	58.2	17.8	30.6	948
890	10.51	7.26	14.0	43.0	59.3	19.3	32.6	953
MEAN	9.79	7.44	13.8	43.9	59.2	18.6	31.4	958
SD	1.227	0.503	0.72	2.53	0.80	0.54	0.84	122.8
N	5	5	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
881	5.3	436.1	15.0	81.9	1.6	1.0	0.3	0.2
882	4.1	325.2	20.2	76.6	1.9	0.8	0.3	0.1
883	6.5	496.7	17.2	80.6	1.3	0.3	0.4	0.2
884	6.3	508.5	13.8	82.7	2.2	0.8	0.3	0.3
885	4.6	373.0	18.0	77.8	2.3	1.0	0.4	0.4
MEAN	5.4	427.9	16.8	79.9	1.9	0.8	0.3	0.2
SD	1.04	78.83	2.52	2.63	0.42	0.29	0.05	0.11
N	5	5	5	5	5	5	5	5

Non-Fasted Females

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
886	4.6	354.8	16.5	81.4	1.1	0.4	0.3	0.3
887	7.9	538.6	20.7	75.3	3.0	0.5	0.3	0.2
888	4.7	346.2	17.0	79.7	2.3	0.5	0.2	0.2
889	4.8	392.8	15.9	79.6	3.2	0.6	0.3	0.3
890	5.4	394.4	28.5	66.8	3.4	0.6	0.4	0.3
MEAN	5.5	405.4	19.7	76.6	2.6	0.5	0.3	0.3
SD	1.39	77.60	5.25	5.90	0.94	0.08	0.07	0.05
N	5	5	5	5	5	5	5	5

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 15

Fasted Females

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM						
881	1.56	8.52	0.17	0.10	0.04	0.02
882	2.20	8.34	0.20	0.09	0.03	0.02
883	1.63	7.63	0.12	0.03	0.04	0.02
884	1.36	8.16	0.21	0.08	0.03	0.03
885	1.70	7.33	0.22	0.10	0.04	0.04
MEAN	1.69	8.00	0.18	0.08	0.04	0.03
SD	0.312	0.499	0.040	0.029	0.005	0.009
N	5	5	5	5	5	5

Non-Fasted Females

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
Group: 3-F:0.150 mg/kg/day CuATSM / H2ATSM						
886	1.48	7.31	0.10	0.04	0.02	0.03
887	2.12	7.72	0.31	0.05	0.03	0.02
888	1.38	6.45	0.19	0.04	0.01	0.02
889	1.77	8.85	0.36	0.06	0.04	0.03
890	2.99	7.02	0.36	0.06	0.04	0.03
MEAN	1.95	7.47	0.26	0.05	0.03	0.03
SD	0.650	0.899	0.115	0.010	0.013	0.005
N	5	5	5	5	5	5

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
806	a	a	a	a	a	a	a	a
807	a	a	a	a	a	a	a	a
808	a	a	a	a	a	a	a	a
809	a	a	a	a	a	a	a	a
810	a	a	a	a	a	a	a	a
811	9.61	7.44	12.4	42.6	57.2	16.6	29.1	1569
812	12.08	9.14	16.0	49.8	54.5	17.5	32.1	815
813	10.54	8.61	15.5	47.4	55.1	18.0	32.7	928
814	11.24	9.12	16.2	50.3	55.2	17.8	32.2	774
815	11.75	9.44	16.2	51.1	54.1	17.1	31.6	847
MEAN	11.04	8.75	15.3	48.2	55.2	17.4	31.5	987
SD	0.990	0.791	1.62	3.44	1.19	0.56	1.42	330.4
N	5	5	5	5	5	5	5	5
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
836	a	a	a	a	a	a	a	a
837	a	a	a	a	a	a	a	a
838	a	a	a	a	a	a	a	a
839	a	a	a	a	a	a	a	a
840	a	a	a	a	a	a	a	a
841	12.07	9.35	16.1	50.7	54.3	17.3	31.8	916
842	11.94	8.84	15.5	48.2	54.5	17.5	32.0	869
843	11.95	9.45	16.4	52.5	55.5	17.3	31.2	876
844	11.56	8.73	15.1	47.9	54.9	17.3	31.5	910
845	11.82	8.98	15.8	48.3	53.8	17.6	32.7	858
MEAN	11.87	9.07	15.8	49.5	54.6	17.4	31.8	886
SD	0.194	0.316	0.51	2.01	0.64	0.14	0.57	25.7
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
806	a	a	a	a	a	a	a	a
807	a	a	a	a	a	a	a	a
808	a	a	a	a	a	a	a	a
809	a	a	a	a	a	a	a	a
810	a	a	a	a	a	a	a	a
811	6.6	492.7	23.0	73.7	2.2	0.3	0.3	0.5
812	2.6	240.6	22.7	72.4	3.0	0.8	0.4	0.7
813	2.2	192.1	19.4	77.2	1.8	0.7	0.4	0.4
814	2.2	198.6	18.1	78.3	2.3	0.6	0.4	0.3
815	2.4	228.0	17.3	78.5	2.4	0.8	0.4	0.7
MEAN	3.2	270.4	20.1	76.0	2.3	0.6	0.4	0.5
SD	1.91	125.89	2.62	2.79	0.43	0.21	0.04	0.18
N	5	5	5	5	5	5	5	5
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM								
836	a	a	a	a	a	a	a	a
837	a	a	a	a	a	a	a	a
838	a	a	a	a	a	a	a	a
839	a	a	a	a	a	a	a	a
840	a	a	a	a	a	a	a	a
841	2.2	203.0	22.7	73.5	2.3	0.6	0.3	0.6
842	2.4	213.3	19.5	76.9	2.0	0.9	0.2	0.5
843	2.5	234.8	17.3	78.6	2.1	0.9	0.5	0.5
844	2.3	203.0	20.8	75.7	2.4	0.6	0.2	0.4
845	1.8	161.5	22.8	71.9	3.5	0.9	0.2	0.7
MEAN	2.2	203.1	20.6	75.3	2.5	0.8	0.3	0.5
SD	0.27	26.64	2.31	2.66	0.60	0.16	0.13	0.11
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 1-M:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
806	a	a	a	a	a	a
807	a	a	a	a	a	a
808	a	a	a	a	a	a
809	a	a	a	a	a	a
810	a	a	a	a	a	a
811	2.21	7.08	0.21	0.03	0.03	0.05
812	2.74	8.75	0.37	0.10	0.05	0.08
813	2.05	8.13	0.19	0.08	0.04	0.04
814	2.03	8.80	0.26	0.06	0.04	0.04
815	2.03	9.23	0.28	0.09	0.05	0.08
MEAN	2.21	8.40	0.26	0.07	0.04	0.06
SD	0.305	0.835	0.070	0.028	0.008	0.020
N	5	5	5	5	5	5
GROUP: 2-M:0.075 mg/kg/day CuATSM / H2ATSM						
836	a	a	a	a	a	a
837	a	a	a	a	a	a
838	a	a	a	a	a	a
839	a	a	a	a	a	a
840	a	a	a	a	a	a
841	2.74	8.87	0.28	0.08	0.04	0.07
842	2.33	9.18	0.24	0.11	0.03	0.06
843	2.07	9.40	0.26	0.11	0.06	0.06
844	2.40	8.75	0.28	0.07	0.03	0.04
845	2.69	8.49	0.41	0.11	0.03	0.09
MEAN	2.45	8.94	0.29	0.10	0.04	0.06
SD	0.275	0.358	0.067	0.019	0.013	0.018
N	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
866	a	a	a	a	a	a	a	a
867	a	a	a	a	a	a	a	a
868	a	a	a	a	a	a	a	a
869	a	a	a	a	a	a	a	a
870	a	a	a	a	a	a	a	a
871	13.56	7.62	13.4	43.4	56.9	17.5	30.8	1414
872	11.01	9.21	15.7	49.7	53.9	17.1	31.7	849
873	11.20	9.20	15.5	50.1	54.5	16.9	31.0	816
874	9.32	9.38	16.1	51.2	54.5	17.2	31.5	929
875	9.28	8.96	15.4	49.3	55.0	17.2	31.3	920
MEAN	10.87	8.87	15.2	48.7	55.0	17.2	31.3	986
SD	1.753	0.717	1.05	3.07	1.15	0.22	0.36	244.2
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM								
866	a	a	a	a	a	a	a	a
867	a	a	a	a	a	a	a	a
868	a	a	a	a	a	a	a	a
869	a	a	a	a	a	a	a	a
870	a	a	a	a	a	a	a	a
871	5.9	449.9	30.4	64.5	3.4	0.5	0.3	0.9
872	2.4	224.9	21.3	74.2	2.7	0.8	0.4	0.7
873	2.2	201.0	18.5	77.2	2.6	0.7	0.4	0.7
874	2.3	216.9	21.3	73.9	3.3	0.5	0.4	0.6
875	1.8	164.1	17.7	79.5	1.6	0.5	0.1	0.5
MEAN	2.9	251.4	21.8	73.9	2.7	0.6	0.3	0.7
SD	1.68	113.42	5.05	5.72	0.72	0.14	0.13	0.15
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: MALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 3-M:0.150 mg/kg/day CuATSM / H2ATSM						
866	a	a	a	a	a	a
867	a	a	a	a	a	a
868	a	a	a	a	a	a
869	a	a	a	a	a	a
870	a	a	a	a	a	a
871	4.12	8.75	0.46	0.07	0.04	0.12
872	2.35	8.17	0.30	0.08	0.04	0.07
873	2.07	8.64	0.29	0.08	0.04	0.08
874	1.99	6.89	0.31	0.05	0.04	0.05
875	1.65	7.38	0.15	0.05	0.01	0.04
MEAN	2.44	7.97	0.30	0.07	0.03	0.07
SD	0.974	0.808	0.110	0.015	0.013	0.031
N	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
821	a	a	a	a	a	a	a	a
822	a	a	a	a	a	a	a	a
823	a	a	a	a	a	a	a	a
824	a	a	a	a	a	a	a	a
825	a	a	a	a	a	a	a	a
826	12.03	7.22	13.7	42.9	59.4	18.9	31.9	616
827	9.18	8.23	15.8	47.8	58.1	19.2	33.0	766
828	10.14	8.46	15.8	49.0	57.9	18.7	32.3	938
829	7.92	8.62	16.4	50.1	58.1	19.1	32.8	840
830	8.99	8.86	16.6	51.2	57.8	18.8	32.5	795
MEAN	9.65	8.28	15.7	48.2	58.3	18.9	32.5	791
SD	1.545	0.635	1.15	3.22	0.65	0.21	0.43	117.6
N	5	5	5	5	5	5	5	5
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
851	a	a	a	a	a	a	a	a
852	a	a	a	a	a	a	a	a
853	a	a	a	a	a	a	a	a
854	a	a	a	a	a	a	a	a
855	a	a	a	a	a	a	a	a
856	10.16	8.01	15.3	47.3	59.0	19.1	32.3	979
857	9.22	8.16	15.6	46.8	57.4	19.1	33.3	840
858	9.77	8.16	15.3	48.0	58.8	18.8	31.9	705
859	9.48	8.44	15.9	49.2	58.3	18.9	32.4	803
860	11.12	8.44	15.6	49.4	58.5	18.5	31.7	905
MEAN	9.95	8.24	15.5	48.1	58.4	18.9	32.3	846
SD	0.741	0.191	0.25	1.14	0.62	0.25	0.62	103.6
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)								
821	a	a	a	a	a	a	a	a
822	a	a	a	a	a	a	a	a
823	a	a	a	a	a	a	a	a
824	a	a	a	a	a	a	a	a
825	a	a	a	a	a	a	a	a
826	5.8	418.4	30.1	64.9	2.7	1.2	0.4	0.6
827	1.9	159.1	22.5	74.5	1.5	0.7	0.4	0.4
828	1.9	162.6	27.8	68.1	2.0	1.0	0.4	0.7
829	1.6	139.4	27.0	69.3	2.1	1.0	0.2	0.5
830	1.7	154.1	19.5	75.8	3.0	0.9	0.4	0.4
MEAN	2.6	206.7	25.4	70.5	2.3	1.0	0.4	0.5
SD	1.80	118.66	4.29	4.55	0.59	0.18	0.09	0.13
N	5	5	5	5	5	5	5	5
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM								
851	a	a	a	a	a	a	a	a
852	a	a	a	a	a	a	a	a
853	a	a	a	a	a	a	a	a
854	a	a	a	a	a	a	a	a
855	a	a	a	a	a	a	a	a
856	1.8	144.5	23.1	72.5	2.5	0.7	0.4	0.7
857	1.8	143.9	21.4	74.2	2.5	0.8	0.4	0.7
858	1.9	153.8	15.6	80.9	1.6	0.5	0.6	0.9
859	1.9	156.7	17.8	77.9	2.6	0.7	0.5	0.5
860	1.9	157.3	18.9	78.5	1.3	0.5	0.3	0.6
MEAN	1.9	151.2	19.4	76.8	2.1	0.6	0.4	0.7
SD	0.05	6.56	2.96	3.40	0.60	0.13	0.11	0.15
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 1-F:0.000 mg/kg/day (0.3% DMSO / 7% ethanol / 92.7% saline)						
821	a	a	a	a	a	a
822	a	a	a	a	a	a
823	a	a	a	a	a	a
824	a	a	a	a	a	a
825	a	a	a	a	a	a
826	3.62	7.80	0.32	0.15	0.05	0.08
827	2.07	6.84	0.14	0.06	0.03	0.04
828	2.82	6.90	0.21	0.10	0.04	0.07
829	2.13	5.49	0.17	0.08	0.02	0.04
830	1.75	6.81	0.27	0.08	0.04	0.04
MEAN	2.48	6.77	0.22	0.09	0.04	0.05
SD	0.748	0.825	0.073	0.034	0.011	0.019
N	5	5	5	5	5	5
GROUP: 2-F:0.075 mg/kg/day CuATSM / H2ATSM						
851	a	a	a	a	a	a
852	a	a	a	a	a	a
853	a	a	a	a	a	a
854	a	a	a	a	a	a
855	a	a	a	a	a	a
856	2.35	7.37	0.26	0.07	0.04	0.07
857	1.97	6.84	0.23	0.08	0.04	0.07
858	1.52	7.90	0.15	0.05	0.05	0.08
859	1.69	7.38	0.25	0.06	0.04	0.05
860	2.11	8.73	0.15	0.05	0.03	0.06
MEAN	1.93	7.64	0.21	0.06	0.04	0.07
SD	0.330	0.713	0.054	0.013	0.007	0.011
N	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	WBC x10e3/uL	RBC x10e6/uL	HGB g/dL	HCT %	MCV fL	MCH pg	MCHC g/dL	PLT x10e3/uL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
881	a	a	a	a	a	a	a	a
882	a	a	a	a	a	a	a	a
883	a	a	a	a	a	a	a	a
884	a	a	a	a	a	a	a	a
885	a	a	a	a	a	a	a	a
886	7.57	8.59	15.5	49.7	57.9	18.0	31.1	806
887	8.37	8.29	16.2	50.0	60.3	19.5	32.4	965
888	10.36	8.07	15.4	46.7	57.9	19.1	32.9	770
889	10.01	8.76	16.1	50.5	57.7	18.4	31.9	939
890	8.88	8.09	15.6	48.0	59.4	19.3	32.5	894
MEAN	9.04	8.36	15.8	49.0	58.6	18.9	32.2	875
SD	1.153	0.306	0.36	1.58	1.15	0.63	0.69	84.2
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	%RETIC %	#RETIC x10e9/L	%NEUT %	%LYMPH %	%MONO %	%EOS %	%BASO %	%LUC %
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM								
881	a	a	a	a	a	a	a	a
882	a	a	a	a	a	a	a	a
883	a	a	a	a	a	a	a	a
884	a	a	a	a	a	a	a	a
885	a	a	a	a	a	a	a	a
886	1.7	144.7	16.2	80.6	1.7	0.9	0.3	0.4
887	1.5	121.3	29.8	66.5	2.1	0.4	0.5	0.6
888	1.9	150.9	20.4	74.5	3.0	0.8	0.6	0.6
889	1.7	147.3	15.7	80.0	2.5	0.9	0.4	0.5
890	1.8	146.3	19.9	75.1	3.6	0.5	0.1	0.9
MEAN	1.7	142.1	20.4	75.3	2.6	0.7	0.4	0.6
SD	0.15	11.85	5.66	5.66	0.75	0.23	0.19	0.19
N	5	5	5	5	5	5	5	5

a - Sacrificed day 15

Appendix C Table C-8 (cont.)

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Day 29

STUDY ID: 2073-002-002 SEX: FEMALE

Animal ID	#NEUT x10e3/uL	#LYMPH x10e3/uL	#MONO x10e3/uL	#EOS x10e3/uL	#BASO x10e3/uL	#LUC x10e3/uL
GROUP: 3-F:0.150 mg/kg/day CuATSM / H2ATSM						
881	a	a	a	a	a	a
882	a	a	a	a	a	a
883	a	a	a	a	a	a
884	a	a	a	a	a	a
885	a	a	a	a	a	a
886	1.22	6.10	0.13	0.07	0.02	0.03
887	2.50	5.57	0.17	0.04	0.04	0.05
888	2.12	7.72	0.31	0.08	0.06	0.07
889	1.58	8.00	0.25	0.09	0.04	0.05
890	1.76	6.66	0.32	0.05	0.01	0.08
MEAN	1.84	6.81	0.24	0.07	0.03	0.06
SD	0.493	1.038	0.084	0.021	0.019	0.019
N	5	5	5	5	5	5

a - Sacrificed day 15

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-9

Individual Animal Bone Marrow Polychromatic Erythrocyte (PCE) Data

Group 1: Vehicle Control (0.00 mg/kg/day CuATSM / H_2ATSM) – Day 15

Animal Number	Sex	%PCE [a]	Micronucleated PCE (MPCE) (Number/2000 PCE Scored)	Log(MPCE+1) [b]
801	M	32.2	0	0.000
802	M	36.2	1	0.301
803	M	53.0	0	0.000
804	M	48.3	0	0.000
805	M	56.3	3	0.602
806	M	60.9	4	0.699
807	M	64.1	5	0.778
808	M	66.9	2	0.477
809	M	70.1	1	0.301
810	M	72.6	1	0.301
	Mean	56.1	2	0.346
	SD	13.78	1.8	0.2904
	N	10	10	10
816	F	52.6	4	0.699
817	F	49.2	1	0.301
818	F	44.8	1	0.301
819	F	57.0	4	0.699
820	F	44.6	2	0.477
821	F	51.3	1	0.301
822	F	56.3	3	0.602
823	F	58.0	4	0.699
824	F	57.9	5	0.778
825	F	56.3	1	0.301
	Mean	52.8	3	0.516
	SD	5.18	1.6	0.2008
	N	10	10	10

[a] %PCE = [(PCE + MPCE) ÷ 1000 erythrocytes] × 100

[b] The counts of micronuclei for each animal were transformed by adding 1 to each count and then the log of the adjusted number was taken and used for statistical comparisons.

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-9 (cont.)

Individual Animal Bone Marrow Polychromatic Erythrocyte (PCE) Data

Group 2: 0.075 mg/kg/day CuATSM / H_2ATSM – Day 15

Animal Number	Sex	%PCE [a]	Micronucleated PCE (MPCE) (Number/2000 PCE Scored)	Log(MPCE+1) [b]
831	M	41.3	2	0.477
832	M	38.6	2	0.477
833	M	57.3	1	0.301
834	M	53.8	2	0.477
835	M	57.6	5	0.778
836	M	61.2	2	0.477
837	M	50.2	4	0.699
838	M	63.3	4	0.699
839	M	63.1	1	0.301
840	M	66.1	3	0.602
	Mean	55.3	3	0.529
	SD	9.36	1.3	0.1633
	N	10	10	10
846	F	55.9	3	0.602
847	F	54.4	2	0.477
848	F	50.4	1	0.301
849	F	46.0	1	0.301
850	F	51.6	2	0.477
851	F	69.5	0	0.000
852	F	53.1	1	0.301
853	F	49.3	6	0.845
854	F	66.8	3	0.602
855	F	59.6	3	0.602
	Mean	55.7	2	0.451
	SD	7.58	1.7	0.2347
	N	10	10	10

[a] %PCE = [(PCE + MPCE) ÷ 1000 erythrocytes] × 100

[b] The counts of micronuclei for each animal were transformed by adding 1 to each count and then the log of the adjusted number was taken and used for statistical comparisons.

Appendix C Table C-9 (cont.)

Individual Animal Bone Marrow Polychromatic Erythrocyte (PCE) Data

Group 3: 0.150 mg/kg/day CuATSM / H_2ATSM – Day 15

Animal Number	Sex	%PCE [a]	Micronucleated PCE (MPCE) (Number/2000 PCE Scored)	Log(MPCE+1) [b]
861	M	42.1	2	0.477
862	M	50.5	0	0.000
863	M	49.8	2	0.477
864	M	46.7	2	0.477
865	M	48.4	4	0.699
866	M	56.0	5	0.778
867	M	61.5	1	0.301
868	M	73.0	3	0.602
869	M	66.3	4	0.699
870	M	54.0	2	0.477
	Mean	54.8	3	0.499
	SD	9.56	1.5	0.2257
	N	10	10	10
876	F	38.0	2	0.477
877	F	50.3	1	0.301
878	F	50.1	4	0.699
879	F	31.9	2	0.477
880	F	45.1	3	0.602
881	F	61.5	2	0.477
882	F	53.0	5	0.778
883	F	58.7	2	0.477
884	F	57.4	5	0.778
885	F	50.1	2	0.477
	Mean	49.6	3	0.554
	SD	9.23	1.4	0.1554
	N	10	10	10

[a] %PCE = [(PCE + MPCE) ÷ 1000 erythrocytes] × 100

[b] The counts of micronuclei for each animal were transformed by adding 1 to each count and then the log of the adjusted number was taken and used for statistical comparisons.

Appendix C Table C-9 (cont.)

Individual Animal Bone Marrow Polychromatic Erythrocyte (PCE) Data

Group 4: Positive Control (30 mg/kg Cyclophosphamide) – Day 15 [a]

Animal Number	Sex	%PCE [b]	Micronucleated PCE (MPCE) (Number/2000 PCE Scored)	Log(MPCE+1) [c]
891	M	35.8	10	1.041
892	M	15.5	8	0.954
893	M	36.6	20	1.322
894	M	32.1	20	1.322
895	M	43.7	15	1.204
	Mean	32.7	15	1.169
	SD	10.51	5.5	0.1663
	N	5	5	5

[a] Positive Control = Cyclophosphamide (30 mg/kg) injected intravenously approximately 24 hours before sacrifice

[b] %PCE = [(PCE + MPCE) ÷ 1000 erythrocytes] × 100

[c] The counts of micronuclei for each animal were transformed by adding 1 to each count and then the log of the adjusted number was taken and used for statistical comparisons.

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-10

Individual Animal Absolute Organ Weights

Group 1: Vehicle Control (0.00 mg/kg/day CuATSM/H_2ATSM) – Day 15

Animal Number	Sex	Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [a]	Thymus	Thyroids [b]
801	M	0.073	1.86	0.92	2.09	9.71	0.58	3.01	0.321	0.016
802	M	0.045	1.76	0.88	1.85	8.28	0.45	2.86	0.231	0.015
803	M	0.051	1.84	0.92	2.03	9.06	0.53	2.83	0.303	0.019
804	M	0.057	1.84	0.79	2.01	9.66	0.53	2.92	0.273	0.020
805	M	0.064	1.84	0.95	2.03	8.86	0.57	2.98	0.271	0.022
806	M	0.046	1.88	0.87	1.99	8.25	0.49	3.01	0.253	0.018
807	M	0.055	1.87	1.00	1.93	8.34	0.54	2.91	0.266	0.019
808	M	0.044	1.79	0.84	1.80	7.73	0.52	2.82	0.302	0.016
809	M	0.066	1.82	1.00	2.02	10.13	0.57	2.86	0.314	0.026
810	M	0.061	1.82	0.83	2.08	9.01	0.52	2.96	0.274	0.018
Mean		0.056	1.83	0.90	1.98	8.90	0.53	2.92	0.281	0.019
SD		0.0098	0.036	0.071	0.095	0.766	0.039	0.072	0.0285	0.0032
N		10	10	10	10	10	10	10	10	10
816	F	0.051	1.69	0.60	1.29	4.81	0.39	0.074	0.256	0.012
817	F	0.056	1.68	0.60	1.36	4.91	0.37	0.088	0.272	0.016
818	F	0.054	1.71	0.63	1.28	5.10	0.36	0.063	0.250	0.015
819	F	0.057	1.77	0.72	1.37	5.57	0.42	0.097	0.318	0.014
820	F	0.059	1.73	0.64	1.39	5.29	0.41	0.066	0.329	0.016
821	F	0.052	1.63	0.64	1.24	4.76	0.32	0.042	0.227	0.013
822	F	0.057	1.70	0.81	1.31	5.04	0.38	0.066	0.267	0.015
823	F	0.064	1.73	0.67	1.26	5.38	0.43	0.124	0.282	0.013
824	F	0.069	1.79	0.65	1.32	5.47	0.43	0.122	0.295	0.015
825	F	0.057	1.67	0.60	1.30	4.79	0.35	0.070	0.256	0.019
Mean		0.058	1.71	0.66	1.31	5.11	0.39	0.081	0.275	0.015
SD		0.0054	0.047	0.066	0.049	0.299	0.037	0.0265	0.0315	0.0020
N		10	10	10	10	10	10	10	10	10

[a] Gonads: Testes for males; Ovaries for females
[b] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-10 (cont.)

Individual Animal Absolute Organ Weights

Group 2: 0.075 mg/kg/day CuATSM/H_2ATSM – Day 15

Animal Number	Sex	Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [a]	Thymus	Thyroids [b]
831	M	0.060	1.77	0.88	1.86	8.93	0.50	2.88	0.365	0.019
832	M	0.049	1.77	0.80	1.72	8.62	0.46	2.71	0.300	0.020
833	M	0.050	1.82	0.87	1.97	8.81	0.50	3.05	0.316	0.021
834	M	0.068	1.86	0.90	2.02	9.58	0.58	2.90	0.384	0.015
835	M	0.056	1.83	0.87	2.15	11.30	0.56	2.97	0.249	0.020
836	M	0.056	1.82	0.91	2.03	10.25	0.51	2.90	0.329	0.010
837	M	0.058	1.81	0.88	1.88	7.59	0.47	2.97	0.270	0.015
838	M	0.054	1.96	0.90	2.07	9.21	0.55	3.10	0.329	0.011
839	M	0.070	1.88	0.87	1.97	8.57	0.49	2.99	0.318	0.013
840	M	0.051	1.82	0.82	2.02	8.50	0.49	2.94	0.250	0.018
Mean		0.057	1.83	0.87	1.97	9.14	0.51	2.94	0.311	0.016
SD		0.0071	0.056	0.035	0.122	1.036	0.040	0.106	0.0451	0.0040
N		10	10	10	10	10	10	10	10	10
846	F	0.057	1.69	0.61	1.33	5.32	0.37	0.059	0.248	0.012
847	F	0.065	1.68	0.63	1.29	4.73	0.40	0.063	0.289	0.016
848	F	0.064	1.72	0.59	1.35	4.85	0.38	0.084	0.253	0.015
849	F	0.069	1.65	0.60	1.26	4.77	0.43	0.080	0.235	0.009
850	F	0.065	1.78	0.68	1.31	5.17	0.41	0.135	0.267	0.011
851	F	0.065	1.70	0.64	1.31	5.50	0.41	0.052	0.321	0.011
852	F	0.065	1.74	0.68	1.24	5.02	0.44	0.088	0.353	0.010
853	F	0.078	1.76	0.63	1.36	5.61	0.42	0.096	0.288	0.014
854	F	0.056	1.71	0.59	1.21	5.04	0.37	0.064	0.244	0.011
855	F	0.078	1.72	0.63	1.36	5.51	0.42	0.080	0.304	0.014
Mean		0.066	1.72	0.63	1.30	5.15	0.41	0.080	0.280	0.012
SD		0.0073	0.038	0.033	0.052	0.322	0.025	0.0239	0.0380	0.0023
N		10	10	10	10	10	10	10	10	10

[a] Gonads: Testes for males; Ovaries for females
[b] Thyroids weighed with parathyroids

Appendix C Table C-10 (cont.)

Individual Animal Absolute Organ Weights

Group 3: 0.150 mg/kg/day CuATSM/H_2ATSM – Day 15

Animal Number	Sex	Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [a]	Thymus	Thyroids [b]
861	M	0.044	1.83	0.95	2.02	10.00	0.52	2.91	0.311	0.018
862	M	0.069	1.80	1.04	2.02	10.41	0.57	2.71	0.262	0.022
863	M	0.053	1.84	0.94	2.03	9.14	0.51	2.95	0.292	0.020
864	M	0.053	1.77	0.94	2.06	10.08	0.56	3.00	0.286	0.016
865	M	0.052	1.83	0.85	1.91	8.92	0.52	2.96	0.238	0.012
866	M	0.047	1.80	0.88	1.92	8.42	0.58	2.94	0.317	0.012
867	M	0.044	1.81	0.78	1.85	8.47	0.53	2.96	0.268	0.011
868	M	0.051	1.85	0.94	1.91	8.18	0.54	2.84	0.265	0.013
869	M	0.053	1.85	0.97	1.94	8.22	0.54	2.81	0.289	0.017
870	M	0.055	1.81	0.83	1.85	8.09	0.51	2.83	0.260	0.011
Mean		0.052	1.82	0.91	1.95	8.99	0.54	2.89	0.279	0.015
SD		0.0071	0.026	0.076	0.076	0.876	0.025	0.090	0.0246	0.0040
N		10	10	10	10	10	10	10	10	10
876	F	0.076	1.77	0.71	1.28	4.87	0.38	0.099	0.291	0.015
877	F	0.058	1.71	0.65	1.25	5.29	0.40	0.088	0.273	0.008
878	F	0.079	1.79	0.64	1.42	5.54	0.44	0.089	0.295	0.018
879	F	0.067	1.77	0.59	1.44	5.17	0.40	0.077	0.278	0.017
880	F	0.074	1.76	0.63	1.42	5.64	0.45	0.090	0.331	0.023
881	F	0.057	1.75	0.65	1.25	4.64	0.35	0.067	0.254	0.014
882	F	0.061	1.78	0.58	1.20	4.85	0.36	0.069	0.276	0.014
883	F	0.052	1.72	0.60	1.29	5.00	0.43	0.064	0.291	0.010
884	F	0.055	1.69	0.64	1.21	4.99	0.36	0.064	0.254	0.014
885	F	0.066	1.69	0.65	1.31	5.41	0.41	0.072	0.241	0.016
Mean		0.065	1.74	0.63	1.31	5.14	0.40	0.078	0.278	0.015
SD		0.0094	0.037	0.037	0.089	0.326	0.035	0.0126	0.0258	0.0041
N		10	10	10	10	10	10	10	10	10

[a] Gonads: Testes for males; Ovaries for females
[b] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-10 (cont.)

Individual Animal Absolute Organ Weights

Group 1: Vehicle Control (0.00 mg/kg/day CuATSM/H_2ATSM) – Day 29

Animal Number	Sex	Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads[a]	Thymus	Thyroids[b]
811	M	0.066	1.83	1.03	1.89	7.60	0.65	2.99	0.282	0.021
812	M	0.064	1.88	1.12	2.01	8.26	0.57	3.03	0.346	0.021
813	M	0.061	1.88	1.06	2.09	8.70	0.61	3.13	0.341	0.020
814	M	0.053	1.91	1.03	1.87	7.83	0.56	3.05	0.259	0.018
815	M	0.038	1.79	0.93	1.86	7.80	0.46	2.37	0.284	0.017
Mean		0.056	1.86	1.03	1.94	8.04	0.57	2.91	0.302	0.019
SD		0.0114	0.048	0.069	0.101	0.441	0.071	0.308	0.0388	0.0018
N		5	5	5	5	5	5	5	5	5
826	F	0.053	1.75	0.72	1.29	7.12	0.49	0.078	0.272	0.016
827	F	0.063	1.76	0.66	1.21	4.76	0.37	0.064	0.287	0.015
828	F	0.053	1.78	0.74	1.39	5.80	0.45	0.072	0.307	0.014
829	F	0.064	1.74	0.75	1.22	5.02	0.38	0.086	0.261	0.020
830	F	0.057	1.79	0.75	1.27	4.96	0.36	0.066	0.235	0.020
Mean		0.058	1.76	0.72	1.28	5.53	0.41	0.073	0.272	0.017
SD		0.0053	0.021	0.038	0.072	0.972	0.057	0.0090	0.0271	0.0028
N		5	5	5	5	5	5	5	5	5

[a] Gonads: Testes for males; Ovaries for females
[b] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-10 (cont.)

Individual Animal Absolute Organ Weights

Group 2: 0.075 mg/kg/day CuATSM/H_2ATSM – Day 29

Animal Number	Sex	Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [a]	Thymus	Thyroids [b]
841	M	0.058	1.90	0.95	1.94	7.93	0.51	3.07	0.304	0.026
842	M	0.050	1.87	1.01	1.99	7.91	0.57	3.11	0.321	0.019
843	M	0.056	1.76	1.00	1.83	7.60	0.54	3.06	0.314	0.020
844	M	0.056	1.82	0.90	1.94	8.62	0.55	2.97	0.282	0.028
845	M	0.066	1.94	1.03	2.12	8.72	0.58	3.27	0.324	0.024
Mean		0.057	1.86	0.98	1.96	8.16	0.55	3.10	0.309	0.023
SD		0.0058	0.070	0.053	0.105	0.488	0.027	0.110	0.0169	0.0038
N		5	5	5	5	5	5	5	5	5
856	F	0.064	1.73	0.67	1.24	5.09	0.41	0.082	0.240	0.017
857	F	0.054	1.75	0.73	1.23	5.05	0.40	0.065	0.256	0.018
858	F	0.062	1.77	0.69	1.39	5.63	0.45	0.077	0.330	0.025
859	F	0.065	1.79	0.71	1.30	5.43	0.39	0.080	0.269	0.016
860	F	0.066	1.78	0.77	1.34	5.15	0.44	0.080	0.301	0.011
Mean		0.062	1.76	0.71	1.30	5.27	0.42	0.077	0.279	0.017
SD		0.0048	0.024	0.038	0.067	0.250	0.026	0.0068	0.0362	0.0050
N		5	5	5	5	5	5	5	5	5

[a] Gonads: Testes for males; Ovaries for females
[b] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-10 (cont.)

Individual Animal Absolute Organ Weights

Group 3: 0.150 mg/kg/day CuATSM/H_2ATSM – Day 29

Animal Number	Sex	Absolute Organ Weight (g)								
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [a]	Thymus	Thyroids [b]
871	M	0.057	1.88	0.93	1.85	7.70	0.58	3.17	0.238	0.024
872	M	0.056	1.93	1.01	1.98	7.90	0.55	3.11	0.313	0.018
873	M	0.049	1.94	0.98	1.98	8.72	0.57	3.18	0.320	0.027
874	M	0.052	1.82	1.00	1.94	8.57	0.54	2.98	0.303	0.022
875	M	0.050	1.90	1.00	1.94	8.80	0.54	3.09	0.350	0.022
Mean		0.053	1.89	0.98	1.94	8.34	0.56	3.11	0.305	0.023
SD		0.0036	0.048	0.032	0.053	0.503	0.018	0.080	0.0413	0.0033
N		5	5	5	5	5	5	5	5	5
886	F	0.049	1.75	0.61	1.14	4.95	0.38	0.084	0.241	0.014
887	F	0.058	1.69	0.65	1.26	4.95	0.38	0.077	0.238	0.019
888	F	0.056	1.76	0.65	1.28	4.77	0.41	0.077	0.239	0.029
889	F	0.052	1.75	0.67	1.23	4.87	0.38	0.074	0.247	0.014
890	F	0.051	1.81	0.70	1.35	5.69	0.44	0.077	0.322	0.015
Mean		0.053	1.75	0.66	1.25	5.05	0.40	0.078	0.257	0.018
SD		0.0037	0.043	0.033	0.077	0.368	0.027	0.0037	0.0363	0.0064
N		5	5	5	5	5	5	5	5	5

[a] Gonads: Testes for males; Ovaries for females
[b] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-11

Individual Animal Organ-to-Body Weight Ratios

Group 1: Vehicle Control (0.00 mg/kg/day CuATSM/H_2ATSM) – Day 15

Animal Number	Sex	Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [b]	Thymus	Thyroids [c]
801	M	238	0.031	0.78	0.39	0.88	4.08	0.24	1.26	0.135	0.007
802	M	218	0.021	0.81	0.40	0.85	3.80	0.21	1.31	0.106	0.007
803	M	229	0.022	0.80	0.40	0.89	3.96	0.23	1.24	0.132	0.008
804	M	225	0.025	0.82	0.35	0.89	4.29	0.24	1.30	0.121	0.009
805	M	230	0.028	0.80	0.41	0.88	3.85	0.25	1.30	0.118	0.010
806	M	230	0.020	0.82	0.38	0.87	3.59	0.21	1.31	0.110	0.008
807	M	230	0.024	0.81	0.43	0.84	3.63	0.23	1.27	0.116	0.008
808	M	217	0.020	0.82	0.39	0.83	3.56	0.24	1.30	0.139	0.007
809	M	235	0.028	0.77	0.43	0.86	4.31	0.24	1.22	0.134	0.011
810	M	231	0.026	0.79	0.36	0.90	3.90	0.23	1.28	0.119	0.008
Mean		228	0.025	0.80	0.39	0.87	3.90	0.23	1.28	0.123	0.008
SD		6.7	0.0038	0.018	0.026	0.023	0.269	0.013	0.031	0.0113	0.0013
N		10	10	10	10	10	10	10	10	10	10
816	F	144	0.035	1.17	0.42	0.90	3.34	0.27	0.051	0.178	0.008
817	F	150	0.037	1.12	0.40	0.91	3.27	0.25	0.059	0.181	0.011
818	F	148	0.036	1.16	0.43	0.86	3.45	0.24	0.043	0.169	0.010
819	F	157	0.036	1.13	0.46	0.87	3.55	0.27	0.062	0.203	0.009
820	F	155	0.038	1.12	0.41	0.90	3.41	0.26	0.043	0.212	0.010
821	F	145	0.036	1.12	0.44	0.86	3.28	0.22	0.029	0.157	0.009
822	F	149	0.038	1.14	0.54	0.88	3.38	0.26	0.044	0.179	0.010
823	F	141	0.045	1.23	0.48	0.89	3.82	0.30	0.088	0.200	0.009
824	F	148	0.047	1.21	0.44	0.89	3.70	0.29	0.082	0.199	0.010
825	F	143	0.040	1.17	0.42	0.91	3.35	0.24	0.049	0.179	0.013
Mean		148	0.039	1.16	0.44	0.89	3.46	0.26	0.055	0.186	0.010
SD		5.1	0.0041	0.039	0.041	0.019	0.182	0.024	0.0183	0.0171	0.0014
N		10	10	10	10	10	10	10	10	10	10

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Gonads: Testes for males; Ovaries for females
[c] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-11 (cont.)

Individual Animal Organ-to-Body Weight Ratios

Group 2: 0.075 mg/kg/day CuATSM/H_2ATSM – Day 15

Animal Number	Sex	Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [b]	Thymus	Thyroids [c]
831	M	213	0.028	0.83	0.41	0.87	4.19	0.23	1.35	0.171	0.009
832	M	212	0.023	0.83	0.38	0.81	4.07	0.22	1.28	0.142	0.009
833	M	231	0.022	0.79	0.38	0.85	3.81	0.22	1.32	0.137	0.009
834	M	231	0.029	0.81	0.39	0.87	4.15	0.25	1.26	0.166	0.006
835	M	245	0.023	0.75	0.36	0.88	4.61	0.23	1.21	0.102	0.008
836	M	241	0.023	0.76	0.38	0.84	4.25	0.21	1.20	0.137	0.004
837	M	220	0.026	0.82	0.40	0.85	3.45	0.21	1.35	0.123	0.007
838	M	226	0.024	0.87	0.40	0.92	4.08	0.24	1.37	0.146	0.005
839	M	216	0.032	0.87	0.40	0.91	3.97	0.23	1.38	0.147	0.006
840	M	221	0.023	0.82	0.37	0.91	3.85	0.22	1.33	0.113	0.008
Mean		226	0.025	0.82	0.39	0.87	4.04	0.23	1.31	0.138	0.007
SD		11.4	0.0033	0.040	0.016	0.035	0.307	0.013	0.065	0.0216	0.0018
N		10	10	10	10	10	10	10	10	10	10
846	F	144	0.040	1.17	0.42	0.92	3.69	0.26	0.041	0.172	0.008
847	F	148	0.044	1.14	0.43	0.87	3.20	0.27	0.043	0.195	0.011
848	F	145	0.044	1.19	0.41	0.93	3.34	0.26	0.058	0.174	0.010
849	F	142	0.049	1.16	0.42	0.89	3.36	0.30	0.056	0.165	0.006
850	F	146	0.045	1.22	0.47	0.90	3.54	0.28	0.092	0.183	0.008
851	F	155	0.042	1.10	0.41	0.85	3.55	0.26	0.034	0.207	0.007
852	F	145	0.045	1.20	0.47	0.86	3.46	0.30	0.061	0.243	0.007
853	F	142	0.055	1.24	0.44	0.96	3.95	0.30	0.068	0.203	0.010
854	F	146	0.038	1.17	0.40	0.83	3.45	0.25	0.044	0.167	0.008
855	F	141	0.055	1.22	0.45	0.96	3.91	0.30	0.057	0.216	0.010
Mean		145	0.046	1.18	0.43	0.90	3.55	0.28	0.055	0.193	0.009
SD		4.0	0.0057	0.042	0.025	0.045	0.243	0.020	0.0166	0.0251	0.0016
N		10	10	10	10	10	10	10	10	10	10

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Gonads: Testes for males; Ovaries for females
[c] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-11 (cont.)

Individual Animal Organ-to-Body Weight Ratios

Group 3: 0.150 mg/kg/day CuATSM/H_2ATSM – Day 15

Animal Number	Sex	Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [b]	Thymus	Thyroids [c]
861	M	241	0.018	0.76	0.39	0.84	4.15	0.22	1.21	0.129	0.007
862	M	242	0.029	0.74	0.43	0.83	4.30	0.24	1.12	0.108	0.009
863	M	229	0.023	0.80	0.41	0.89	3.99	0.22	1.29	0.128	0.009
864	M	249	0.021	0.71	0.38	0.83	4.05	0.22	1.20	0.115	0.006
865	M	222	0.023	0.82	0.38	0.86	4.02	0.23	1.33	0.107	0.005
866	M	223	0.021	0.81	0.39	0.86	3.78	0.26	1.32	0.142	0.005
867	M	224	0.020	0.81	0.35	0.83	3.78	0.24	1.32	0.120	0.005
868	M	217	0.024	0.85	0.43	0.88	3.77	0.25	1.31	0.122	0.006
869	M	222	0.024	0.83	0.44	0.87	3.70	0.24	1.27	0.130	0.008
870	M	221	0.025	0.82	0.38	0.84	3.66	0.23	1.28	0.118	0.005
Mean		229	0.023	0.80	0.40	0.85	3.92	0.24	1.27	0.122	0.007
SD		11.0	0.0030	0.044	0.029	0.022	0.213	0.014	0.068	0.0107	0.0016
N		10	10	10	10	10	10	10	10	10	10
876	F	147	0.052	1.20	0.48	0.87	3.31	0.26	0.067	0.198	0.010
877	F	149	0.039	1.15	0.44	0.84	3.55	0.27	0.059	0.183	0.005
878	F	155	0.051	1.15	0.41	0.92	3.57	0.28	0.057	0.190	0.012
879	F	149	0.045	1.19	0.40	0.97	3.47	0.27	0.052	0.187	0.011
880	F	154	0.048	1.14	0.41	0.92	3.66	0.29	0.058	0.215	0.015
881	F	151	0.038	1.16	0.43	0.83	3.07	0.23	0.044	0.168	0.009
882	F	145	0.042	1.23	0.40	0.83	3.34	0.25	0.048	0.190	0.010
883	F	147	0.035	1.17	0.41	0.88	3.40	0.29	0.044	0.198	0.007
884	F	140	0.039	1.21	0.46	0.86	3.56	0.26	0.046	0.181	0.010
885	F	144	0.046	1.17	0.45	0.91	3.76	0.28	0.050	0.167	0.011
Mean		148	0.044	1.18	0.43	0.88	3.47	0.27	0.053	0.188	0.010
SD		4.6	0.0058	0.029	0.028	0.046	0.198	0.019	0.0076	0.0143	0.0027
N		10	10	10	10	10	10	10	10	10	10

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Gonads: Testes for males; Ovaries for females
[c] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-11 (cont.)

Individual Animal Organ-to-Body Weight Ratios

Group 1: Vehicle Control (0.00 mg/kg/day CuATSM/H_2ATSM) – Day 29

Animal Number	Sex	Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [b]	Thymus	Thyroids [c]
811	M	236	0.028	0.78	0.44	0.80	3.22	0.28	1.27	0.119	0.009
812	M	249	0.026	0.76	0.45	0.81	3.32	0.23	1.22	0.139	0.008
813	M	268	0.023	0.70	0.40	0.78	3.25	0.23	1.17	0.127	0.007
814	M	246	0.022	0.78	0.42	0.76	3.18	0.23	1.24	0.105	0.007
815	M	243	0.016	0.74	0.38	0.77	3.21	0.19	0.98	0.117	0.007
Mean		248	0.023	0.75	0.42	0.78	3.24	0.23	1.18	0.121	0.008
SD		12.0	0.0046	0.033	0.029	0.021	0.053	0.032	0.115	0.0126	0.0009
N		5	5	5	5	5	5	5	5	5	5
826	F	155	0.034	1.13	0.46	0.83	4.59	0.32	0.050	0.175	0.010
827	F	151	0.042	1.17	0.44	0.80	3.15	0.25	0.042	0.190	0.010
828	F	169	0.031	1.05	0.44	0.82	3.43	0.27	0.043	0.182	0.008
829	F	155	0.041	1.12	0.48	0.79	3.24	0.25	0.055	0.168	0.013
830	F	153	0.037	1.17	0.49	0.83	3.24	0.24	0.043	0.154	0.013
Mean		157	0.037	1.13	0.46	0.81	3.53	0.27	0.047	0.174	0.011
SD		7.1	0.0046	0.049	0.023	0.018	0.601	0.032	0.0057	0.0138	0.0022
N		5	5	5	5	5	5	5	5	5	5

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Gonads: Testes for males; Ovaries for females
[c] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-11 (cont.)

Individual Animal Organ-to-Body Weight Ratios

Group 2: 0.075 mg/kg/day CuATSM/H_2ATSM – Day 29

Animal Number	Sex	Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [b]	Thymus	Thyroids [c]
841	M	255	0.023	0.75	0.37	0.76	3.11	0.20	1.20	0.119	0.010
842	M	257	0.019	0.73	0.39	0.77	3.08	0.22	1.21	0.125	0.007
843	M	248	0.023	0.71	0.40	0.74	3.06	0.22	1.23	0.127	0.008
844	M	258	0.022	0.71	0.35	0.75	3.34	0.21	1.15	0.109	0.011
845	M	264	0.025	0.73	0.39	0.80	3.30	0.22	1.24	0.123	0.009
Mean		256	0.022	0.73	0.38	0.76	3.18	0.21	1.21	0.121	0.009
SD		5.8	0.0022	0.017	0.020	0.023	0.132	0.009	0.035	0.0071	0.0016
N		5	5	5	5	5	5	5	5	5	5
856	F	155	0.041	1.12	0.43	0.80	3.28	0.26	0.053	0.155	0.011
857	F	148	0.036	1.18	0.49	0.83	3.41	0.27	0.044	0.173	0.012
858	F	157	0.039	1.13	0.44	0.89	3.59	0.29	0.049	0.210	0.016
859	F	166	0.039	1.08	0.43	0.78	3.27	0.23	0.048	0.162	0.010
860	F	165	0.040	1.08	0.47	0.81	3.12	0.27	0.048	0.182	0.007
Mean		158	0.039	1.12	0.45	0.82	3.33	0.26	0.048	0.176	0.011
SD		7.5	0.0019	0.041	0.027	0.042	0.176	0.022	0.0032	0.0214	0.0033
N		5	5	5	5	5	5	5	5	5	5

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Gonads: Testes for males; Ovaries for females
[c] Thyroids weighed with parathyroids

14-DAY TOXICITY STUDY OF CuATSM / H_2ATSM (NSC-D729307) IN RATS

Appendix C Table C-11 (cont.)

Individual Animal Organ-to-Body Weight Ratios

Group 3: 0.150 mg/kg/day CuATSM/H_2ATSM – Day 29

Animal Number	Sex	Fasted Body Weight (g)	Organ-to-Body Weight Ratio (%) [a]								
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Gonads [b]	Thymus	Thyroids [c]
871	M	234	0.024	0.80	0.40	0.79	3.29	0.25	1.35	0.102	0.010
872	M	256	0.022	0.75	0.39	0.77	3.09	0.21	1.21	0.122	0.007
873	M	250	0.020	0.78	0.39	0.79	3.49	0.23	1.27	0.128	0.011
874	M	252	0.021	0.72	0.40	0.77	3.40	0.21	1.18	0.120	0.009
875	M	255	0.020	0.75	0.39	0.76	3.45	0.21	1.21	0.137	0.009
Mean		249	0.021	0.76	0.39	0.78	3.34	0.22	1.24	0.122	0.009
SD		8.9	0.0017	0.031	0.005	0.013	0.161	0.018	0.068	0.0129	0.0015
N		5	5	5	5	5	5	5	5	5	5
886	F	145	0.034	1.21	0.42	0.79	3.41	0.26	0.058	0.166	0.010
887	F	150	0.039	1.13	0.43	0.84	3.30	0.25	0.051	0.159	0.013
888	F	159	0.035	1.11	0.41	0.81	3.00	0.26	0.048	0.150	0.018
889	F	153	0.034	1.14	0.44	0.80	3.18	0.25	0.048	0.161	0.009
890	F	165	0.031	1.10	0.42	0.82	3.45	0.27	0.047	0.195	0.009
Mean		154	0.035	1.14	0.42	0.81	3.27	0.26	0.050	0.166	0.012
SD		7.8	0.0029	0.043	0.011	0.019	0.183	0.008	0.0045	0.0171	0.0038
N		5	5	5	5	5	5	5	5	5	5

[a] Organ-to-Body Weight Ratio = [Absolute Organ Weight (g) ÷ Fasted Body Weight (g)] × 100
[b] Gonads: Testes for males; Ovaries for females
[c] Thyroids weighed with parathyroids

Appendix D: Pathology Report

FINAL PATHOLOGY REPORT FOR
14-DAY TOXICITY STUDY OF CuATSM/H_2ATSM (NSC-D729307) IN RATS
IITRI PROJECT NUMBER 2073-002-002

PREPARED
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NOVEMBER 10, 2004

Final Pathology Report
IIT Research Institute
Project Number 2073-002-002

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IIT Research Institute
Project Number 2073-002-002

SECTION I

PATHOLOGY NARRATIVE

FINAL PATHOLOGY REPORT

14-DAY TOXICITY STUDY OF CuATSM/H_2ATSM (NSC-D729307) IN RATS

INTRODUCTION

This pathology report, submitted by Pathology Associates Division of Charles River Laboratories, Inc. to IIT Research Institute (IITRI), represents the histopathology findings for the study designated as "14-Day Toxicity Study of CuATSM/H_2ATSM (NSC-D729307) in Rats," IITRI Project Number 2073-002-002.

The study was conducted to determine target organ toxicity of CuATSM/H_2ATSM (NSC-D729307) and its reversibility given intravenously to rats once a day for 14 days.

EXPERIMENTAL DESIGN AND METHODS

This study was composed of 4 groups. Groups 1, 2 and 3 were composed of 15 male and 15 female Fischer 344[CDF(F-344)/CrlBR] rats. Group 4 was composed of 10 male Fischer 344[CDF(F-344)/CrlBR] rats. Ten rats/sex/group from Groups 1, 2, and 3 were sacrificed on study day 15 (terminal necropsy) and the remaining 5/sex/group were observed for an additional 15 days and were sacrificed on study day 29 (recovery necropsy). Five rats from Group 4 were sacrificed on day 15 (terminal necropsy) and the remaining 5 animals from Group 4 were sacrificed on day 29 (recovery necropsy). Group 1 animals received the test article vehicle by intravenous injection at a dose volume of 5 mL/kg/day for 14 consecutive days. Animals in Groups 2 and 3 were given the test article (at targeted doses of 0.075 and 0.150 mg/kg/day, respectively) by slow bolus intravenous injection once a day for 14 consecutive days at a dose volume of 5 mL/kg/day. Group 4 animals were used as a positive control group for *in vivo* mutagenicity assessment. Group 4 animals received an intravenous injection of cyclophosphamide (30 mg/kg) at a dose volume of 2 mL/kg/day on study days 14 or 28 and were euthanized approximately 18-24 hours after injection on study days 15 or 29, respectively. Animals from Group 4 were not subjected to necropsy. The experimental design is summarized in Table I (Summary of Experimental Design).

Animals from Groups 1, 2 and 3 were euthanized and necropsied on study day 15 or 29. All necropsies were performed according to IITRI Standard Operating Procedures. Scheduled sacrifice necropsies were conducted by Pathology Associates Division of Charles River Laboratories, Inc. personnel. Tissues required by the protocol (see Table II, Protocol-Required Tissues) were examined and placed in 10% neutral buffered formalin, with the exception of eyes and harderian gland which were placed in Davidson's fixative and testes and epididymides which were placed in Bouin's fixative. Femoral bone marrow smears were prepared and fixed from terminal sacrifice animals taken from the right femur, but myeloid:erythroid ratios were not

determined. The micronucleus assay, performed by IITRI personnel, evaluated bone marrow from the left femur.

Tissues required for histopathologic evaluation were trimmed, processed, sectioned, and stained with hematoxylin and eosin in accordance with Pathology Associates Division of Charles River Laboratories, Inc. Standard Operating Procedures. All protocol required tissues from the terminal sacrifice Group 1 and Group 3 animals were processed and evaluated. Some tissues are inherently difficult to obtain in sections because of their small size (e.g. parathyroid gland). Tissues were recorded as "unavailable/unsuitable for complete evaluation" when they were missing in both the original section and in recut and/or retrim attempts to obtain them.

The cassettes containing the testes and epididymides from Group 2 animal number 831 and Group 3 animal number 868 were both found open after fixation. Both sets of testes were processed to slides for microscopic evaluation. Microscopically, both sets of testes were normal and thus an "N" was entered into the LabCat database for testes for animal number 868. One set of epididymides contained minimal chronic inflammation and one was normal. As animal identification was unclear, a "U" was entered into the LabCat database for epididymides for animal number 868 data.

Histopathologic observations were tabulated using the LABCAT® histopathology data management system (version 4.33). Microscopic findings for all groups are summarized in the Project Summary reports (Section II). Where applicable, all tissue changes received a severity grade based upon the following scale: 1 = minimal, 2 = mild, 3 = moderate and 4 = marked. Mean group severity scores (SEV) for each change were determined by dividing the sum of the severity scores by the number of tissues examined in that group. The mean group severity scores are found in the Severity Summary reports (Section III). Microscopic findings in the protocol-required tissues for individual animals are presented in the Tabulated Animal Data reports (Section IV). The correlation of the necropsy findings and histopathology findings are reported in the Correlation of Gross and Microscopic (Micro) Findings reports (Section V). The codes used as entries in these tables are explained in the Reports Code Table.

The portion of this study performed by Pathology Associates Division of Charles River Laboratories, Inc. was conducted in compliance with the U.S. Food and Drug Administration's Good Laboratory Practice (GLP) regulations for nonclinical studies (21 CFR Part 58).

RESULTS AND DISCUSSION

The Results and Discussion section is divided into three parts: Necropsy Findings, Diagnostic Terms, and Histopathology Findings. The Necropsy Findings portion describes lesions seen at necropsy and trimming. The Diagnostic Terms portion lists and clarifies diagnostic terminology that may be unclear. The Histopathology Findings portion of this section reports the results and provides discussion of the histopathologic evaluation of the tissues.

Necropsy Findings

All gross lesions observed in this study were interpreted as incidental findings typically present in rat toxicology studies. Gross observations are summarized in Tables IIIA (Day 15) and IIIB (Day 29), Summary of Gross Necropsy Observations and listed in the Correlation of Gross and Microscopic (Micro) Findings report in Section V. Microscopic findings were correlated with gross lesions when possible.

Diagnostic Terms

The diagnoses used in this study were considered to be self-explanatory and were not discussed in this section.

Histopathology Findings

There were no treatment-related histopathologic findings in the tissues required to be examined by the protocol from Groups 1 and 3 terminal sacrifice animals. All microscopic findings were interpreted as incidental findings that are commonly present in rat toxicology studies.

CONCLUSIONS

Under conditions of this study, a daily dose of CuATSM/H_2ATSM for 14 days by intravenous injection to rats at a targeted dose of 0.150 mg/kg/day resulted in no histologic treatment-related findings. The no observed effect level (NOEL) in this 14 day intravenous study was 0.150 mg/kg/day.

Carol J. Detrisac, DVM, PhD
Diplomate, ACVP

11/10/04
Date

TABLE I
SUMMARY OF EXPERIMENTAL DESIGN

Group Number	Daily Dose CuATSM/H_2ATSM		Number of Rats at Study Start (M + F)	Number of Rats	
	mg/kg/day	mg/m^2/day		Day 15 (M + F)	Day 29 (M + F)
1 (VCTL)	0.000	0.00	15 + 15	10 + 10	5 + 5
2	0.075	0.45	15 + 15	10 +10	5 + 5
3	0.150	0.90	15 + 15	10 + 10	5 + 5
4	Cyclophosphamide (30 mg/kg)		10 + 0	5 + 0	5 + 0

VCTL = Vehicle Control

TABLE II
PROTOCOL-REQUIRED TISSUES

Adrenal glands
Brain (entire)
Epididymides
Esophagus
Eyes
Femur (bone and marrow)
Harderian Gland
Heart
Kidneys
Large intestine (cecum and colon)
Liver
Lungs
Lymph nodes (mandibular and mesenteric)
Mammary gland (when present in regular abdominal skin section)
Ovaries
Pancreas
Pituitary gland
Salivary gland (mandibular, sublingual, and parotid)
Sciatic nerve
Skeletal muscle (biceps femoris)
Skin (injection site)
Small intestines (duodenum, jejunum, and ileum)
Spinal cord (thoracolumbar)
Spleen
Stomach
Testes
Thymus
Thyroid gland with parathyroids
Trachea
Urinary bladder
Uterus
Gross lesions

TABLE IIIA (DAY 15)
SUMMARY OF GROSS NECROPSY OBSERVATIONS [a]

	Group 1		Group 2		Group 3	
	M	F	M	F	M	F
Number of animals examined	10	10	10	10	10	10
Tissue/Lesion						
Eye						
Pigmentation	--	1	--	1	--	--
Small	--	--	--	1	--	--
Liver						
Mass	--	--	1	--	1	--
Lung						
Focus	1	--	--	--	--	--
Lymph Node, Mandibular						
Pigmentation	--	--	--	--	1	--
Skin, Tail						
Crust	--	--	--	1	--	--
Thymus						
Pigmentation	3	--	7	--	5	--
Uterus, Horn						
Dilatation	--	1	--	--	--	--

[a] = Number of animals in which each lesion was observed
-- = No signs observed
Group 1 = 0.000 mg/kg/day
Group 2 = 0.075 mg/kg/day
Group 3 = 0.150 mg/kg

TABLE IIIB (DAY 29)
SUMMARY OF GROSS NECROPSY OBSERVATIONS [a]

	Group 1		Group 2		Group 3	
	M	F	M	F	M	F
Number of animals examined	5	5	5	5	5	5
Tissue/Lesion						
Eye						
Pigmentation	--	--	--	1	1	--
Liver						
Mass	--	1	--	--	--	--
Lymph Node, Mandibular						
Enlarged	--	--	--	--	1	--
Skin						
Crust	--	--	--	--	1	--
Skin, Tail						
Pigmentation	--	--	1	--	--	--
Testes						
Small	1	--	--	--	--	--
Thymus						
Pigmentation	1	--	--	--	1	--

[a] = Number of animals in which each lesion was observed
-- = No signs observed
Group 1 = 0.000 mg/kg/day
Group 2 = 0.075 mg/kg/day
Group 3 = 0.150 mg/kg

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Reports Code Table

A. Codes applying to organs

N	Tissues within normal histological limits
A	Autolysis precluding adequate evaluation
U	Tissues unavailable/unsuitable for complete evaluation

B. Codes applying to microscopic diagnoses

1	minimal
2	mild
3	moderate
4	marked
P	Present
I	Bilateral
L	Unilateral
-	No data entered

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SECTION II

PROJECT SUMMARY

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		3	
		(1)		(2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
BRAIN	# EX	10		10	
SPINAL CORD,THORACOLUMBAR	# EX	10		10	
SALIVARY GLAND,MANDIBULAR	# EX	10		10	
SALIVARY GLAND,SUBLINGUAL	# EX	10		10	
SALIVARY GLAND,PAROTID	# EX	10		9	
LYMPH NODE,MANDIBULAR	# EX	10		10	
Hyperplasia		3	30.0	0	0.0
PANCREAS	# EX	10		10	
THYMUS	# EX	10		10	
Hemorrhage, acute		7	70.0	4	40.0
PERIPHERAL NERVE,SCIATIC	# EX	10		10	
THYROID GLAND	# EX	10		10	
PARATHYROID GLAND	# EX	7		9	
ESOPHAGUS	# EX	10		10	
TRACHEA	# EX	10		10	
Inflammation, chronic		2	20.0	1	10.0
ADRENAL GLAND	# EX	10		10	
Vacuolation, cortex		1	10.0	4	40.0

Incidence Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		3	
		(1)		(2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
PITUITARY GLAND	# EX	10		10	
Cyst		2	20.0	4	40.0
HEART	# EX	10		10	
Cardiomyopathy		4	40.0	2	20.0
SKELETAL MUSCLE	# EX	10		10	
SPLEEN	# EX	10		10	
STOMACH	# EX	10		10	
Mineralization, mucosa		4	40.0	7	70.0
SMALL INTESTINE,DUODENUM	# EX	10		10	
SMALL INTESTINE,ILEUM	# EX	10		10	
LARGE INTESTINE,COLON	# EX	10		10	
MAMMARY GLAND	# EX	8		9	
LARGE INTESTINE,CECUM	# EX	10		10	
SMALL INTESTINE,JEJUNUM	# EX	10		10	
LYMPH NODE,MESENTERIC	# EX	10		10	
LIVER	# EX	10		10	
Inflammation, chronic		7	70.0	8	80.0
Hepatodiaphragmatic nodule		0	0.0	1	10.0
SKIN,INJECTION SITE	# EX	10		10	
Crust, serocellular		3	30.0	0	0.0

Incidence Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1 (1)		3 (2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
SKIN, INJECTION SITE	# EX	10		10	
Fibrosis, dermis		1	10.0	0	0.0
Fibrin deposition, dermis		1	10.0	1	10.0
Inflammation, chronic, dermis		0	0.0	1	10.0
LUNG	# EX	10		10	
Inflammation, chronic		1	10.0	0	0.0
Ectopic bone		2	20.0	0	0.0
Granuloma		2	20.0	3	30.0
Embolus		0	0.0	1	10.0
Inflammation, acute		0	0.0	1	10.0
Hemorrhage, acute		1	10.0	0	0.0
KIDNEY	# EX	10		10	
Mineralization, cortex		10	100.0	10	100.0
Mineralization, medulla		5	50.0	7	70.0
Nephropathy		1	10.0	0	0.0
URINARY BLADDER	# EX	10		10	
TESTES	# EX	10		10	
EPIDIDYMIS	# EX	10		9	
Inflammation, chronic		0	0.0	1	11.1
HARDERIAN GLAND	# EX	10		10	
Inflammation, chronic		0	0.0	1	10.0
EYE	# EX	10		10	
Mineralization, cornea		4	40.0	3	30.0
Mineralization, conjunctiva		1	10.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - 0.00 mg/kg/day (Vehicle Control)
(2) - 0.150 mg/kg/day (High Dose)

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14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		3	
		(1)		(2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
BONE,FEMUR	# EX	10		10	
Mineralization, periosteum		5	50.0	2	20.0
BONE MARROW,FEMORAL	# EX	10		10	
SKIN	# EX	10		10	

Incidence Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1 (1)		3 (2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
BRAIN	# EX	10		10	
Hemorrhage, optic nerve		0	0.0	1	10.0
SPINAL CORD,THORACOLUMBAR	# EX	10		10	
SALIVARY GLAND,MANDIBULAR	# EX	10		10	
Metaplasia, mucous		0	0.0	1	10.0
SALIVARY GLAND,SUBLINGUAL	# EX	10		10	
SALIVARY GLAND,PAROTID	# EX	10		10	
LYMPH NODE,MANDIBULAR	# EX	10		10	
PANCREAS	# EX	10		10	
Inflammation, chronic		0	0.0	1	10.0
THYMUS	# EX	10		10	
Depletion, lymphocyte		3	30.0	4	40.0
PERIPHERAL NERVE,SCIATIC	# EX	9		10	
THYROID GLAND	# EX	10		10	
PARATHYROID GLAND	# EX	7		9	
ESOPHAGUS	# EX	10		10	
TRACHEA	# EX	10		10	
Inflammation, chronic		3	30.0	2	20.0
ADRENAL GLAND	# EX	10		10	

Incidence Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
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IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1 (1)		3 (2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
PITUITARY GLAND	# EX	10		10	
Cyst		4	40.0	5	50.0
HEART	# EX	10		10	
Cardiomyopathy		1	10.0	0	0.0
SKELETAL MUSCLE	# EX	10		10	
SPLEEN	# EX	10		10	
STOMACH	# EX	10		10	
Ectopic pancreas		0	0.0	1	10.0
SMALL INTESTINE,DUODENUM	# EX	10		10	
SMALL INTESTINE,ILEUM	# EX	10		10	
LARGE INTESTINE,COLON	# EX	10		10	
Inflammation, chronic		1	10.0	0	0.0
MAMMARY GLAND	# EX	8		10	
LARGE INTESTINE,CECUM	# EX	10		10	
Inflammation, chronic		0	0.0	1	10.0
SMALL INTESTINE,JEJUNUM	# EX	10		10	
LYMPH NODE,MESENTERIC	# EX	10		10	
Hyperplasia		1	10.0	2	20.0
LIVER	# EX	10		10	
Inflammation, chronic		9	90.0	10	100.0
Necrosis, individual cell		1	10.0	0	0.0

Incidence Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		3	
		(1)		(2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
SKIN, INJECTION SITE	# EX	10		10	
Crust, serocellular		1	10.0	3	30.0
Fibrin deposition, dermis		3	30.0	1	10.0
Inflammation, chronic, dermis		3	30.0	1	10.0
Inflammation, acute, dermis		1	10.0	0	0.0
Dyskeratosis, epidermis		1	10.0	0	0.0
Hyperplasia, epidermis		0	0.0	1	10.0
LUNG	# EX	10		10	
Inflammation, chronic		3	30.0	1	10.0
Granuloma		3	30.0	4	40.0
Embolus		0	0.0	1	10.0
Inflammation, acute		0	0.0	2	20.0
Hemorrhage, acute		1	10.0	0	0.0
Histiocytosis, alveolar		1	10.0	1	10.0
KIDNEY	# EX	10		10	
Mineralization, cortex		10	100.0	10	100.0
Mineralization, medulla		10	100.0	10	100.0
URINARY BLADDER	# EX	10		10	
OVARY	# EX	10		10	
UTERUS	# EX	10		10	
Dilation		6	60.0	3	30.0
HARDERIAN GLAND	# EX	10		10	
EYE	# EX	10		10	
Mineralization, cornea		4	40.0	4	40.0
Degeneration, retina		0	0.0	1	10.0
Gliosis, optic nerve		0	0.0	1	10.0

Incidence Calculated by No. of Tissues Scored
(1) - 0.00 mg/kg/day (Vehicle Control)
(2) - 0.150 mg/kg/day (High Dose)

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14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
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PROJECT SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		1		3	
		(1)		(2)	
NUMBER OF ANIMALS:		10		10	
		#	%	#	%
BONE,FEMUR	# EX	10		10	
Mineralization, periosteum		3	30.0	1	10.0
BONE MARROW,FEMORAL	# EX	10		10	
SKIN	# EX	10		10	

Incidence Calculated by No. of Tissues Scored
(1) - 0.00 mg/kg/day (Vehicle Control)
(2) - 0.150 mg/kg/day (High Dose)

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SECTION III

SEVERITY SUMMARY

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

SEVERITY SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: MALE

GROUP:		1 (1)	3 (2)
NUMBER OF ANIMALS:		10	10
		# SEV	# SEV
BRAIN	# EX	10	10
SPINAL CORD,THORACOLUMBAR	# EX	10	10
SALIVARY GLAND,MANDIBULAR	# EX	10	10
SALIVARY GLAND,SUBLINGUAL	# EX	10	10
SALIVARY GLAND,PAROTID	# EX	10	9
LYMPH NODE,MANDIBULAR	# EX	10	10
Hyperplasia		3 0.30	0 0.00
PANCREAS	# EX	10	10
THYMUS	# EX	10	10
Hemorrhage, acute		7 0.80	4 0.50
PERIPHERAL NERVE,SCIATIC	# EX	10	10
THYROID GLAND	# EX	10	10
PARATHYROID GLAND	# EX	7	9
ESOPHAGUS	# EX	10	10
TRACHEA	# EX	10	10
Inflammation, chronic		2 0.20	1 0.10
ADRENAL GLAND	# EX	10	10
Vacuolation, cortex		1 0.10	4 0.40
PITUITARY GLAND	# EX	10	10
Cyst		2 0.20	4 0.40

Severity Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

SEVERITY SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: MALE

GROUP:	1 (1)	3 (2)
NUMBER OF ANIMALS:	10	10
	# SEV	# SEV
HEART	# EX 10	10
Cardiomyopathy	4 0.40	2 0.20
SKELETAL MUSCLE	# EX 10	10
SPLEEN	# EX 10	10
STOMACH	# EX 10	10
Mineralization, mucosa	4 0.40	7 0.70
SMALL INTESTINE,DUODENUM	# EX 10	10
SMALL INTESTINE,ILEUM	# EX 10	10
LARGE INTESTINE,COLON	# EX 10	10
MAMMARY GLAND	# EX 8	9
LARGE INTESTINE,CECUM	# EX 10	10
SMALL INTESTINE,JEJUNUM	# EX 10	10
LYMPH NODE,MESENTERIC	# EX 10	10
LIVER	# EX 10	10
Inflammation, chronic	7 0.70	8 0.80
Hepatodiaphragmatic nodule	0 0.00	1 0.20
SKIN,INJECTION SITE	# EX 10	10
Crust, serocellular	3 0.30	0 0.00
Fibrosis, dermis	1 0.10	0 0.00
Fibrin deposition, dermis	1 0.10	1 0.10
Inflammation, chronic, dermis	0 0.00	1 0.10

Severity Calculated by No. of Tissues Scored
(1) - 0.00 mg/kg/day (Vehicle Control)
(2) - 0.150 mg/kg/day (High Dose)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

SEVERITY SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: MALE

GROUP:	1 (1)	3 (2)
NUMBER OF ANIMALS:	10	10
	# SEV	# SEV
LUNG	# EX 10	10
Inflammation, chronic	1 0.10	0 0.00
Ectopic bone	2 0.20	0 0.00
Granuloma	2 0.20	3 0.30
Embolus	0 0.00	1 0.10
Inflammation, acute	0 0.00	1 0.10
Hemorrhage, acute	1 0.10	0 0.00
KIDNEY	# EX 10	10
Mineralization, cortex	10 1.20	10 1.10
Mineralization, medulla	5 0.50	7 0.70
Nephropathy	1 0.10	0 0.00
URINARY BLADDER	# EX 10	10
TESTES	# EX 10	10
EPIDIDYMIS	# EX 10	9
Inflammation, chronic	0 0.00	1 0.11
HARDERIAN GLAND	# EX 10	10
Inflammation, chronic	0 0.00	1 0.20
EYE	# EX 10	10
Mineralization, cornea	4 0.40	3 0.30
Mineralization, conjunctiva	1 0.10	0 0.00
BONE,FEMUR	# EX 10	10
Mineralization, periosteum	5 0.50	2 0.20
BONE MARROW,FEMORAL	# EX 10	10
SKIN	# EX 10	10

Severity Calculated by No. of Tissues Scored
(1) - 0.00 mg/kg/day (Vehicle Control)
(2) - 0.150 mg/kg/day (High Dose)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

SEVERITY SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

GROUP:		1	3
		(1)	(2)
NUMBER OF ANIMALS:		10	10
		# SEV	# SEV
BRAIN	# EX	10	10
Hemorrhage, optic nerve		0 0.00	1 0.10
SPINAL CORD,THORACOLUMBAR	# EX	10	10
SALIVARY GLAND,MANDIBULAR	# EX	10	10
Metaplasia, mucous		0 0.00	1 0.10
SALIVARY GLAND,SUBLINGUAL	# EX	10	10
SALIVARY GLAND,PAROTID	# EX	10	10
LYMPH NODE,MANDIBULAR	# EX	10	10
PANCREAS	# EX	10	10
Inflammation, chronic		0 0.00	1 0.10
THYMUS	# EX	10	10
Depletion, lymphocyte		3 0.30	4 0.40
PERIPHERAL NERVE,SCIATIC	# EX	9	10
THYROID GLAND	# EX	10	10
PARATHYROID GLAND	# EX	7	9
ESOPHAGUS	# EX	10	10
TRACHEA	# EX	10	10
Inflammation, chronic		3 0.30	2 0.20
ADRENAL GLAND	# EX	10	10

Severity Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

SEVERITY SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

GROUP:	1	3
	(1)	(2)
NUMBER OF ANIMALS:	10	10
	# SEV	# SEV
PITUITARY GLAND	# EX 10	10
Cyst	4 0.40	5 0.50
HEART	# EX 10	10
Cardiomyopathy	1 0.10	0 0.00
SKELETAL MUSCLE	# EX 10	10
SPLEEN	# EX 10	10
STOMACH	# EX 10	10
Ectopic pancreas	0 0.00	1 0.20
SMALL INTESTINE,DUODENUM	# EX 10	10
SMALL INTESTINE,ILEUM	# EX 10	10
LARGE INTESTINE,COLON	# EX 10	10
Inflammation, chronic	1 0.10	0 0.00
MAMMARY GLAND	# EX 8	10
LARGE INTESTINE,CECUM	# EX 10	10
Inflammation, chronic	0 0.00	1 0.10
SMALL INTESTINE,JEJUNUM	# EX 10	10
LYMPH NODE,MESENTERIC	# EX 10	10
Hyperplasia	1 0.10	2 0.20
LIVER	# EX 10	10
Inflammation, chronic	9 0.90	10 1.00
Necrosis, individual cell	1 0.10	0 0.00

Severity Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

SEVERITY SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

GROUP:	1	3
	(1)	(2)
NUMBER OF ANIMALS:	10	10

		#	SEV	#	SEV
SKIN,INJECTION SITE	# EX	10		10	
Crust, serocellular		1	0.10	3	0.40
Fibrin deposition, dermis		3	0.30	1	0.20
Inflammation, chronic, dermis		3	0.30	1	0.10
Inflammation, acute, dermis		1	0.10	0	0.00
Dyskeratosis, epidermis		1	0.10	0	0.00
Hyperplasia, epidermis		0	0.00	1	0.20
LUNG	# EX	10		10	
Inflammation, chronic		3	0.30	1	0.10
Granuloma		3	0.30	4	0.40
Embolus		0	0.00	1	0.10
Inflammation, acute		0	0.00	2	0.20
Hemorrhage, acute		1	0.10	0	0.00
Histiocytosis, alveolar		1	0.10	1	0.10
KIDNEY	# EX	10		10	
Mineralization, cortex		10	1.00	10	1.00
Mineralization, medulla		10	1.00	10	1.00
URINARY BLADDER	# EX	10		10	
OVARY	# EX	10		10	
UTERUS	# EX	10		10	
Dilation		6	1.20	3	0.70
HARDERIAN GLAND	# EX	10		10	
EYE	# EX	10		10	
Mineralization, cornea		4	0.40	4	0.40
Degeneration, retina		0	0.00	1	0.20
Gliosis, optic nerve		0	0.00	1	0.10

Severity Calculated by No. of Tissues Scored (2) - 0.150 mg/kg/day (High Dose)
(1) - 0.00 mg/kg/day (Vehicle Control)

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

SEVERITY SUMMARY

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15 SEX: FEMALE

GROUP:	1 (1)	3 (2)
NUMBER OF ANIMALS:	10	10
	# SEV	# SEV
BONE,FEMUR # EX	10	10
Mineralization, periosteum	3 0.30	1 0.10
BONE MARROW,FEMORAL # EX	10	10
SKIN # EX	10	10

Severity Calculated by No. of Tissues Scored
(1) - 0.00 mg/kg/day (Vehicle Control)
(2) - 0.150 mg/kg/day (High Dose)

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SECTION IV

TABULATED ANIMAL DATA

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 1: 0.00 mg/kg/day (Vehicle Control)
DAYS ON TEST: 15-15 SEX: MALE

ANIMAL ID:	801	802	803	804	805	806	807	808	809	810
BRAIN	N	N	N	N	N	N	N	N	N	N
SPINAL CORD,THORACOLUMBAR	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,MANDIBULAR	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,SUBLINGUAL	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,PAROTID	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MANDIBULAR	N	-	N	N	N	N	N	N	-	-
Hyperplasia	-	1	-	-	-	-	-	-	1	1
PANCREAS	N	N	N	N	N	N	N	N	N	N
THYMUS	-	-	-	N	-	N	-	N	-	-
Hemorrhage, acute	1	1	1	-	1	-	2	-	1	1
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	U	N	N	U	N	N	U	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	-	N	N	N	N	N	-	N	N
Inflammation, chronic	-	1	-	-	-	-	-	1	-	-
ADRENAL GLAND	N	N	N	N	-	N	N	N	N	N
Vacuolation, cortex	-	-	-	-	1	-	-	-	-	-
PITUITARY GLAND	N	N	-	N	N	N	-	N	N	N
Cyst	-	-	1	-	-	-	1	-	-	-

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 1: 0.00 mg/kg/day (Vehicle Control)
DAYS ON TEST: 15-15 SEX: MALE

ANIMAL ID:	801	802	803	804	805	806	807	808	809	810
HEART	N	N	N	N	N	-	-	N	-	-
Cardiomyopathy	-	-	-	-	-	1	1	-	1	1
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SPLEEN	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	-	N	N	-	N	N	-	-
Mineralization, mucosa	-	-	1	-	-	1	-	-	1	1
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,ILEUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	U	N	U
LARGE INTESTINE,CECUM	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	N	N	N	N
LIVER	N	-	N	N	-	-	-	-	-	-
Inflammation, chronic	-	1	-	-	1	1	1	1	1	1
SKIN,INJECTION SITE	N	N	-	-	-	N	N	-	N	-
Crust, serocellular	-	-	1	-	-	-	-	1	-	1
Fibrosis, dermis	-	-	-	1	-	-	-	-	-	-
Fibrin deposition, dermis	-	-	-	-	1	-	-	-	-	-
LUNG	-	N	-	N	N	-	-	N	-	-
Inflammation, chronic	-	-	1	-	-	-	-	-	-	-
Ectopic bone	-	-	-	-	-	1	1	-	-	-
Granuloma	1	-	-	-	-	-	-	-	1	-

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 1: 0.00 mg/kg/day (Vehicle Control)
DAYS ON TEST: 15-15 SEX: MALE

ANIMAL ID:	801	802	803	804	805	806	807	808	809	810
Hemorrhage, acute	-	-	-	-	-	-	-	-	-	1
KIDNEY	-	-	-	-	-	-	-	-	-	-
Mineralization, cortex	2	1	2	1	1	1	1	1	1	1
Mineralization, medulla	1	1	-	1	1	-	1	-	-	-
Nephropathy	-	1	-	-	-	-	-	-	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N	N	N	N	N	N
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
EYE	N	N	-	N	-	N	-	N	-	N
Mineralization, cornea	-	-	1	-	1	-	1	-	1	-
Mineralization, conjunctiva	-	-	1	-	-	-	-	-	-	-
BONE,FEMUR	-	-	-	-	N	-	N	N	N	N
Mineralization, periosteum	1	1	1	1	-	1	-	-	-	-
BONE MARROW,FEMORAL	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 3: 0.150 mg/kg/day (High Dose)
DAYS ON TEST: 15-15 SEX: MALE

ANIMAL ID:	861	862	863	864	865	866	867	868	869	870
BRAIN	N	N	N	N	N	N	N	N	N	N
SPINAL CORD,THORACOLUMBAR	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,MANDIBULAR	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,SUBLINGUAL	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,PAROTID	N	N	N	N	N	N	N	U	N	N
LYMPH NODE,MANDIBULAR	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	-	N	-	-	-	N	N	N
Hemorrhage, acute	-	-	1	-	1	2	1	-	-	-
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	U	N	N	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	N	N	N	N	N	N	-	N	N
Inflammation, chronic	-	-	-	-	-	-	-	1	-	-
ADRENAL GLAND	-	-	-	N	N	N	N	-	N	N
Vacuolation, cortex	1	1	1	-	-	-	-	1	-	-
PITUITARY GLAND	N	-	N	-	N	N	N	-	N	-
Cyst	-	1	-	1	-	-	-	1	-	1
HEART	N	-	N	N	N	N	-	N	N	N
Cardiomyopathy	-	1	-	-	-	-	1	-	-	-

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 3: 0.150 mg/kg/day (High Dose)
DAYS ON TEST: 15-15 SEX: MALE

ANIMAL ID:	861	862	863	864	865	866	867	868	869	870
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SPLEEN	N	N	N	N	N	N	N	N	N	N
STOMACH	-	-	-	-	-	-	N	-	N	N
Mineralization, mucosa	1	1	1	1	1	1	-	1	-	-
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,ILEUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	U	N	N	N	N
LARGE INTESTINE,CECUM	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	N	N	N	N
LIVER	-	-	-	-	-	-	N	-	-	-
Inflammation, chronic	1	1	-	1	1	1	-	1	1	1
Hepatodiaphragmatic nodule	-	-	2	-	-	-	-	-	-	-
SKIN,INJECTION SITE	N	N	N	N	-	N	N	N	-	N
Fibrin deposition, dermis	-	-	-	-	1	-	-	-	-	-
Inflammation, chronic, dermis	-	-	-	-	-	-	-	-	1	-
LUNG	-	N	N	-	-	N	N	-	N	N
Granuloma	1	-	-	1	-	-	-	1	-	-
Embolus	-	-	-	-	1	-	-	-	-	-
Inflammation, acute	-	-	-	-	1	-	-	-	-	-
KIDNEY	-	-	-	-	-	-	-	-	-	-
Mineralization, cortex	1	1	2	1	1	1	1	1	1	1

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 3: 0.150 mg/kg/day (High Dose)
DAYS ON TEST: 15-15 SEX: MALE

ANIMAL ID:	861	862	863	864	865	866	867	868	869	870
Mineralization, medulla	1	1	1	1	1	1	-	1	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	N
EPIDIDYMIS	N	N	N	N	N	N	N	U	-	N
Inflammation, chronic	-	-	-	-	-	-	-	-	1	-
HARDERIAN GLAND	N	N	N	N	N	N	N	N	-	N
Inflammation, chronic	-	-	-	-	-	-	-	-	2	-
EYE	-	N	N	-	N	N	N	N	-	N
Mineralization, cornea	1	-	-	1	-	-	-	-	1	-
BONE,FEMUR	N	-	-	N	N	N	N	N	N	N
Mineralization, periosteum	-	1	1	-	-	-	-	-	-	-
BONE MARROW,FEMORAL	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 1: 0.00 mg/kg/day (Vehicle Control)
DAYS ON TEST: 15-15 SEX: FEMALE

ANIMAL ID:	816	817	818	819	820	821	822	823	824	825
BRAIN	N	N	N	N	N	N	N	N	N	N
SPINAL CORD,THORACOLUMBAR	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,MANDIBULAR	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,SUBLINGUAL	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,PAROTID	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MANDIBULAR	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N	N	N	-	-	-
Depletion, lymphocyte	-	-	-	-	-	-	-	1	1	1
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	U
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	U	N	N	U	U	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	-	N	-	N	N	N	N	N	-
Inflammation, chronic	-	1	-	1	-	-	-	-	-	1
ADRENAL GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	-	N	N	N	-	-	-
Cyst	-	-	-	1	-	-	-	1	1	1
HEART	N	N	N	-	N	N	N	N	N	N
Cardiomyopathy	-	-	-	1	-	-	-	-	-	-

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15

STUDY NUMBER: 2073
GROUP: 1: 0.00 mg/kg/day (Vehicle Control)
SEX: FEMALE

ANIMAL ID:	816	817	818	819	820	821	822	823	824	825
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SPLEEN	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,ILEUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	-	N
Inflammation, chronic	-	-	-	-	-	-	-	-	1	-
MAMMARY GLAND	N	U	N	N	N	N	N	N	N	U
LARGE INTESTINE,CECUM	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	N	-	N	N
Hyperplasia	-	-	-	-	-	-	-	1	-	-
LIVER	-	-	-	-	-	-	-	-	-	N
Inflammation, chronic	1	1	1	1	1	1	1	1	1	-
Necrosis, individual cell	-	-	1	-	-	-	-	-	-	-
SKIN,INJECTION SITE	-	-	-	N	N	-	N	N	N	N
Crust, serocellular	-	-	-	-	-	1	-	-	-	-
Fibrin deposition, dermis	1	1	1	-	-	-	-	-	-	-
Inflammation, chronic, dermis	1	-	1	-	-	1	-	-	-	-
Inflammation, acute, dermis	-	1	-	-	-	-	-	-	-	-
Dyskeratosis, epidermis	-	-	1	-	-	-	-	-	-	-
LUNG	-	-	-	-	-	N	N	-	-	N
Inflammation, chronic	1	1	-	-	-	-	-	1	-	-
Granuloma	-	1	1	1	-	-	-	-	-	-

See Reports Code Table for Symbol Definitions

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14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15

STUDY NUMBER: 2073
GROUP: 1: 0.00 mg/kg/day (Vehicle Control)
SEX: FEMALE

ANIMAL ID:	816	817	818	819	820	821	822	823	824	825
Hemorrhage, acute	-	-	-	-	1	-	-	-	-	-
Histiocytosis, alveolar	-	-	-	-	-	-	-	-	1	-
KIDNEY	-	-	-	-	-	-	-	-	-	-
Mineralization, cortex	1	1	1	1	1	1	1	1	1	1
Mineralization, medulla	1	1	1	1	1	1	1	1	1	1
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N
UTERUS	N	-	N	-	-	-	N	N	-	-
Dilation	-	2	-	2	3	2	-	-	1	2
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
EYE	N	N	-	N	-	N	N	-	N	-
Mineralization, cornea	-	-	1	-	1	-	-	1	-	1
BONE,FEMUR	-	N	N	N	N	N	-	N	-	N
Mineralization, periosteum	1	-	-	-	-	-	1	-	1	-
BONE MARROW,FEMORAL	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15

STUDY NUMBER: 2073
GROUP: 3: 0.150 mg/kg/day (High Dose)
SEX: FEMALE

ANIMAL ID:	876	877	878	879	880	881	882	883	884	885
BRAIN	N	N	N	N	N	N	N	N	N	-
Hemorrhage, optic nerve	-	-	-	-	-	-	-	-	-	1
SPINAL CORD,THORACOLUMBAR	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,MANDIBULAR	N	-	N	N	N	N	N	N	N	N
Metaplasia, mucous	-	1	-	-	-	-	-	-	-	-
SALIVARY GLAND,SUBLINGUAL	N	N	N	N	N	N	N	N	N	N
SALIVARY GLAND,PAROTID	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MANDIBULAR	N	N	N	N	N	N	N	N	N	N
PANCREAS	N	N	N	-	N	N	N	N	N	N
Inflammation, chronic	-	-	-	1	-	-	-	-	-	-
THYMUS	N	N	N	N	N	N	-	-	-	-
Depletion, lymphocyte	-	-	-	-	-	-	1	1	1	1
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	U	N	N
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	N	-	N	N	N	N	N	N	N	-
Inflammation, chronic	-	1	-	-	-	-	-	-	-	1
ADRENAL GLAND	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	-	N	-	N	-	N	N	N	-	-
Cyst	1	-	1	-	1	-	-	-	1	1

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IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002 STUDY NUMBER: 2073
FATE: Terminal Sacrifice GROUP: 3: 0.150 mg/kg/day (High Dose)
DAYS ON TEST: 15-15 SEX: FEMALE

ANIMAL ID:	876	877	878	879	880	881	882	883	884	885
HEART	N	N	N	N	N	N	N	N	N	N
SKELETAL MUSCLE	N	N	N	N	N	N	N	N	N	N
SPLEEN	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	-	N	N	N	N
Ectopic pancreas	-	-	-	-	-	2	-	-	-	-
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,ILEUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	N	N
MAMMARY GLAND	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,CECUM	N	N	N	-	N	N	N	N	N	N
Inflammation, chronic	-	-	-	1	-	-	-	-	-	-
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	-	N	-	N
Hyperplasia	-	-	-	-	-	-	1	-	1	-
LIVER	-	-	-	-	-	-	-	-	-	-
Inflammation, chronic	1	1	1	1	1	1	1	1	1	1
SKIN,INJECTION SITE	N	N	-	N	-	N	-	-	N	N
Crust, serocellular	-	-	1	-	-	-	1	2	-	-
Fibrin deposition, dermis	-	-	-	-	-	-	-	2	-	-
Inflammation, chronic, dermis	-	-	-	-	1	-	-	-	-	-
Hyperplasia, epidermis	-	-	-	-	-	-	-	2	-	-
LUNG	-	-	-	N	N	N	N	-	-	N
Inflammation, chronic	-	-	-	-	-	-	-	-	1	-

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

TABULATED ANIMAL DATA

STUDY ID : 2073-002-002
FATE: Terminal Sacrifice
DAYS ON TEST: 15-15

STUDY NUMBER: 2073
GROUP: 3: 0.150 mg/kg/day (High Dose)
SEX: FEMALE

ANIMAL ID:	876	877	878	879	880	881	882	883	884	885
Granuloma	-	1	1	-	-	-	-	1	1	-
Embolus	1	-	-	-	-	-	-	-	-	-
Inflammation, acute	1	1	-	-	-	-	-	-	-	-
Histiocytosis, alveolar	-	-	-	-	-	-	-	1	-	-
KIDNEY	-	-	-	-	-	-	-	-	-	-
Mineralization, cortex	1	1	1	1	1	1	1	1	1	1
Mineralization, medulla	1	1	1	1	1	1	1	1	1	1
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N	N	N	N
UTERUS	N	N	N	N	N	-	N	-	-	N
Dilation	-	-	-	-	-	3	-	2	2	-
HARDERIAN GLAND	N	N	N	N	N	N	N	N	N	N
EYE	N	N	N	-	-	-	-	-	N	N
Mineralization, cornea	-	-	-	1	1	1	-	1	-	-
Degeneration, retina	-	-	-	-	-	-	2	-	-	-
Gliosis, optic nerve	-	-	-	-	-	-	-	1	-	-
BONE,FEMUR	-	N	N	N	N	N	N	N	N	N
Mineralization, periosteum	1	-	-	-	-	-	-	-	-	-
BONE MARROW,FEMORAL	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N	N	N	N	N	N

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Final Pathology Report
IIT Research Institute
Project Number 2073-002-002

SECTION V

CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002
STUDY NUMBER: 2073
SEX: MALE
GROUP: 1: 0.00 mg/kg/day (Vehicle Control)

Animal ID: 801
Animal Fate: Terminal Sacrifice
Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, RED	THYMUS - Hemorrhage, acute

Animal ID: 803
Animal Fate: Terminal Sacrifice
Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, RED	THYMUS - Hemorrhage, acute

Animal ID: 807
Animal Fate: Terminal Sacrifice
Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - UNILATERAL, PIGMENTATION, MOTTLED	THYMUS - Hemorrhage, acute

Animal ID: 808
Animal Fate: Terminal Sacrifice
Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
LUNG - LEFT, FOCUS, 3x3 MM, RED	LUNG - No corresponding lesion

Animal ID: 814
Animal Fate: Recovery Sacrifice
Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, MOTTLED, RED	THYMUS - Not required by protocol

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002
STUDY NUMBER: 2073
SEX: MALE
GROUP: 1: 0.00 mg/kg/day (Vehicle Control)

Animal ID: 815
Animal Fate: Recovery Sacrifice
Days on Test: 29

Reference to Necropsy Record:
TESTES - LEFT, SMALL

Related Histopathology:
TESTES - Not required by protocol

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002 STUDY NUMBER: 2073
SEX: MALE GROUP: 2: 0.075 mg/kg/day (Low Dose)

Animal ID: 831
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - BILATERAL, PIGMENTATION, MOTTLED	THYMUS - Not required by protocol

Animal ID: 832
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - BILATERAL, PIGMENTATION, MOTTLED, RED	THYMUS - Not required by protocol

Animal ID: 833
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, MOTTLED	THYMUS - Not required by protocol

Animal ID: 834
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, MOTTLED	THYMUS - Not required by protocol

Animal ID: 837
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
LIVER - MEDIAN LOBE, MASS, 5x5x2 MM	LIVER - Not required by protocol
THYMUS - PIGMENTATION, MOTTLED	THYMUS - Not required by protocol

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002 STUDY NUMBER: 2073
SEX: MALE GROUP: 2: 0.075 mg/kg/day (Low Dose)

Animal ID: 838
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, MOTTLED	THYMUS - Not required by protocol

Animal ID: 840
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - UNILATERAL, PIGMENTATION, RED	THYMUS - Not required by protocol

Animal ID: 844
Animal Fate: Recovery Sacrifice Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,TAIL - PIGMENTATION, 5x3 MM, BLACK	SKIN,TAIL - Not required by protocol

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002 STUDY NUMBER: 2073
SEX: MALE GROUP: 3: 0.150 mg/kg/day (High Dose)

Animal ID: 863
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
LIVER - MEDIAN LOBE, MASS, 13x10x3 MM (Adhered to diaphragm)	LIVER - Hepatodiaphragmatic nodule
THYMUS - PIGMENTATION, RED	THYMUS - Hemorrhage, acute

Animal ID: 865
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, MOTTLED	THYMUS - Hemorrhage, acute

Animal ID: 866
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, RED	THYMUS - Hemorrhage, acute

Animal ID: 867
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, MOTTLED, RED	THYMUS - Hemorrhage, acute

Animal ID: 869
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
LYMPH NODE,MANDIBULAR - PIGMENTATION, RED	LYMPH NODE,MANDIBULAR - No corresponding lesion

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PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002 STUDY NUMBER: 2073
SEX: MALE GROUP: 3: 0.150 mg/kg/day (High Dose)

Animal ID: 870
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, RED	THYMUS - No corresponding lesion

Animal ID: 871
Animal Fate: Recovery Sacrifice Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
LYMPH NODE,MANDIBULAR - ENLARGED, MULTIPLE	LYMPH NODE,MANDIBULAR - Not required by protocol
EYE - RIGHT, PIGMENTATION, RED	EYE - Not requested by protocol
SKIN - LIP, RIGHT, CRUST, 6x5 MM (Ulcerated)	SKIN - Not required by protocol

Animal ID: 875
Animal Fate: Recovery Sacrifice Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
THYMUS - UNILATERAL, PIGMENTATION, DARK	THYMUS - Not required by protocol

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002 STUDY NUMBER: 2073
SEX: FEMALE GROUP: 1: 0.00 mg/kg/day (Vehicle Control)

Animal ID: 820
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
UTERUS - HORN, BILATERAL, DILATATION	UTERUS - Dilation

Animal ID: 824
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
EYE - UNILATERAL, PIGMENTATION, DARK	EYE - No corresponding lesion

Animal ID: 826
Animal Fate: Recovery Sacrifice Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
LIVER - CAUDATE LOBE, MASS, 20x10x8 MM, DARK	LIVER - Not required by protocol

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002 STUDY NUMBER: 2073
SEX: FEMALE GROUP: 2: 0.075 mg/kg/day (Low Dose)

Animal ID: 846
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
SKIN,INJECTION SITE - TAIL, CRUST, 40x4x4 MM, DARK	SKIN,INJECTION SITE - Not required by protocol

Animal ID: 854
Animal Fate: Terminal Sacrifice Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
EYE - RIGHT, SMALL	EYE - Not required by protocol
EYE - RIGHT, PIGMENTATION, RED	EYE - Not required by protocol

Animal ID: 856
Animal Fate: Recovery Sacrifice Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
EYE - RIGHT, PIGMENTATION, OPAQUE	EYE - Not required by protocol

PATHOLOGY ASSOCIATES DIVISION OF CHARLES RIVER LABORATORIES, INC.
14-DAY TOXICITY STUDY OF CuATSM/H2ATSM (NSC-D729307) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 2073-002-002

CORRELATION OF GROSS & MICRO

STUDY ID: 2073-002-002 STUDY NUMBER: 2073

SEX: FEMALE GROUP: 3: 0.150 mg/kg/day (High Dose)

No Gross Observations for any animal in this group

SECTION VI

QUALITY ASSURANCE STATEMENT

QUALITY ASSURANCE STATEMENT

This histopathology project was inspected and audited by the Pathology Associates Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) standards promulgated by the U.S. Food and Drug Administration. The following table is a record of the inspections/audits performed and reported by the QAU:

Date of Inspection	Phase Inspected	Date Findings Reported to Management and Study Pathologist	Date Findings Reported to Study Director and Study Director Facility Management
06/07/04	Quality Control	06/11/04	06/11/04
07/20/04	Individual Animal Data	07/23/04	07/23/04
07/20,21/04	Draft Pathology Report	07/23/04	07/23/04
11/10/04	Final Pathology Report	11/10/04	11/10/04

Enosha Simmons
Enosha Simmons
Quality Assurance Unit
Pathology Associates Illinois Division

11/10/2004
Date