8EHQ-0201-14400

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International Business Machines Corporation

Route 100
Somers, NY 10589

8EHQ-99-14400

Global Occupational Health Services
Human Resources
(914)766-0266

January 31, 2001

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Mr. Richard H. Hefter
Document Control Office (7407)
Room G99 East Tower, Attention: Section 8(e)
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
401 "M" Street, S.W.
Washington, D.C. 20460-0001

Contain NO CBI

Subject: TSCA Section 8(e) Disclosure Follow Up, 8EHQ-0399-14400

Dear Mr. Hefter:

This letter is intended as a follow up to our initial submission to you dated March 10, 1999, as well as respond to your recently received requests for additional information. Pursuant to Section 8(e) of the Toxic Substances Control Act, 15 U.S.C. Section 2607(e), International Business Machines Corporation (IBM) submits the following information on tetramethylammonium hydroxide, CAS number 75-59-2 (TMAH).

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Within the United States, TMAH is used at IBM sites in East Fishkill, New York; Poughkeepsie, New York; Yorktown Heights, New York; Essex Junction, Vermont; Rochester, Minnesota; San Jose, California; and Tucson, Arizona. TMAH is primarily used in dilute aqueous solutions, in concentrations ranging from less than 1% to 25%, in semiconductor package manufacturing cleaning operations and in semiconductor photolithography processes.

In anticipation of further expanding our use of TMAH, IBM sponsored toxicity testing of TMAH on rats to provide information on potential dermal toxicity. Preliminary results from this study, reported to you on March 10, 1999, indicate that longer term or repeated exposure of rats' skin to concentrations of TMAH as low as 5% in distilled water may produce significant systemic toxicity, including death. The final report of this study, generated by IBM's contracted laboratory, IIT Research Institute, Chicago, Illinois, is attached. (Attachment #1)

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IBM has taken a number of actions as a result of these preliminary data and observations.

1) We have updated electronic material safety data sheets in use in IBM for TMAH and TMAH-containing substances to reflect the new information. An example is attached. (Attachment #2)

2) IBM's medical and industrial hygiene professionals notified employees and contractors who work with TMAH at IBM facilities. This included re-enforcement of existing work practices. An example of the portion of a site specific communication that includes work practice information is attached. (Attachment #3)

3) Concurrent with the earlier TSCA 8(e) notification, we have provided our TMAH suppliers (Attachment #4) with a summary of IBM's toxicity testing results and informed the Chemical Manufacturers Association (CMA) and Semiconductor Industry Association (SIA) of these preliminary findings.

4) Additionally, we have sponsored permeation testing of certain glove types using standard method ASTM F-739-96, the results of which are attached. (Attachment #5). IBM will use Solvex or Trionic Gloves.

5) IBM has sponsored two additional investigations into TMAH toxicity. These were conducted at IBM's contracted laboratory, IIT Research Institute, Chicago, Illinois.

The first of the additional studies was designed to determine the length of time a 25% concentration of TMAH in distilled water, applied dermally at a dose of 1 mg/kg, could remain on the skin of rats prior to inducing a lethal systemic effect. The study also attempted to determine if cholinergic disturbances were responsible for the observed systemic toxicity. A brief summary of the study design and the preliminary results follows.

Six groups of male and female rats were dermally exposed to a 25% concentration of TMAH in distilled water. The test material was administered at a constant volume of 1 mg/kg, placed in a small flat Hill Top chamber firmly affixed to a shaved area of the animal's back. The first 5 groups consisted of 3 rats/sex/group. Each group was exposed to 25% TMAH in distilled water for a time interval of 15 minutes, 30 minutes, 45 minutes, 1 hour, or 2 hours. The skin of each animal was washed with water to remove any residual test substance after the specified exposure time interval. A sixth group consisted of 9 rats/sex/group and was dermally exposed to a 25% concentration of TMAH in distilled water for 3 hours. This group was further divided into three subsets of 3 rats/sex/group. The first subset was not washed following test substance exposure. The second subset was designated for determination of acetylcholinesterase activity levels in erythrocytes and plasma.

These rats were removed from the study prior to determination of mortality. The third subset was designated for injection with atropine sulfate (administered approximately 0.5 hours prior to dermal exposure to TMAH) to determine if the significant systemic toxicity could be counteracted by competitive inhibition of muscarinic acetylcholine receptors. A seventh group of 3 rats/sex/group was exposed to deionized water and served as a vehicle control.

In groups 1 through 5, mortality was observed in 2 of 3 males exposed to a 25% solution of TMAH in distilled water for 30 minutes, 0 males at 45 minutes, 3 of 3 males in the 1- and 2-hour exposure groups. Conversely, mortality was noted in only 1 of 3 females in the 45 minute and 1 hour exposure groups, and 2 of 3 females in the 2 hour exposure group. All mortalities occurred 1 to 2 hours after dosing with the exception of 1 male rat in the 30 minute exposure group that died on day 2. All rats in the 15 minute exposure group survived and did not exhibit overt signs of toxicity. It appears that male rats were more sensitive to the effects of TMAH exposure than female rats. Specifically, 8 of 12 male rats died in the groups exposed to TMAH for 2 hours or less in comparison to 4 of 12 female rats in the same treatment groups.

All of the rats in the sixth group, dermally exposed to 25% TMAH in distilled water for 3 hours, died within 2 hours, including those rats treated with atropine sulfate. Thus atropine sulfate did not protect rats from the systemic effects of TMAH. Acetylcholinesterase activity in erythrocytes and plasma was unaffected by TMAH exposure. A final report for this study has been attached. (Attachment #6)

The second additional investigation was designed to confirm the results of IBM's first TMAH study, to focus study on a tighter dose grouping, and to determine if either a cholinergic effect or blood gas disturbance may be underlying mechanisms in the observed systemic effects following dermal applications. A brief summary of the study design and results follows.

Six groups of 10 male and 10 female rats were dermally exposed to 0%, 0.25%, 0.55%, 1.0%, 3% and 5% concentrations of TMAH in distilled water. A seventh group of 10 male and 10 female rats were exposed to a 5% concentration of sodium hydroxide (NaOH) in water, and served as a positive base control. The test materials were administered at a constant volume of 1 ml/kg, placed in a small flat Hill Top chamber firmly affixed to a shaved area of the animal's back. Exposures were to occur for 6 hours/day, 5 days/week, for 4 weeks. However, the NaOH positive control group was treated for only two days (female) or three days (male) prior to being euthanized due to the corrosiveness of the 5% NaOH formulation. Necropsy was not performed on the NaOH positive control group.

Three additional groups of male and female rats were dermally exposed to 0%, 5% and 25% solutions of TMAH in distilled water in an effort to determine

blood gas and hematology profiles for TMAH exposed animals. Six male and six female rats were dermally exposed to 0% or 5% TMAH in distilled water and 8 male and 8 female rats were dermally exposed to 25% TMAH in distilled water for 1 to 4 hours prior to blood collection under anesthesia to measure blood gas and hematology parameters.

All of the rats dermally exposed to a 5% solution of TMAH in distilled water died within the first three days, with the exception of 1 female and 1 male that died eight days following exposure. Mortality was observed in 8 of 10 male and female rats dermally exposed to a 3% solution of TMAH in distilled water. These deaths occurred between 1 and 14 days following exposure. None of the rats dermally exposed to 0%, 0.25%, 0.55% and 1% TMAH solutions died, and no overt signs of systemic toxicity were observed in these groups. However, signs of dermal irritation were observed in male and female rats treated with TMAH solutions at concentrations of 0.55% and above.

A significant decrease in pH and an increase in PCO_2 were observed in both male and female rats treated with a 25% solution of TMAH in distilled water. Furthermore, male rats treated with the 25% TMAH solution also had decreased HCO_3. Rats treated with a 5% TMAH solution had only decreased PO_2 levels. These disturbances in blood gases may at least partially explain the deaths noted in rats dermally exposed to 3% and 5% TMAH solutions.

No toxicologically significant effects were noted on body weight gain, organ weights, food consumption, hematology, urinalysis, and acetylcholinesterase activity in male or female rats treated with TMAH solutions. Test substance-related histopathological changes were observed in the skin of the application site, and the lung, thymus and liver. Skin lesions at the application site consisted of necrosis, squamous epithelial hyperplasia, exudative scabs and inflammation. In the liver, vacuolation (male rats), eosinophilic intraplasmic material (male and female rats), and individual hepatocyte necrosis (male rats) were considered to be treatment related. Pulmonary congestion, associated with pulmonary compromise, was noted in rats that died after dermal exposure to a 3% TMAH solution. Thymic lymphoid necrosis noted in the rats treated with a 3% TMAH solution was attributed to stress.

Based on the results of this study, the no observed adverse effect level (NOAEL) for systemic toxicity due to dermal exposure due to a 1% TMAH solution, equated to an approximate dose of 10 mg/kg. The NOAEL for dermal irritation resulting from exposure to a TMAH solution is 0.55% in males and 0.25% in females. These equate to approximate doses of 5.5 mg/kg and 2.5 mg/kg respectively. The final report for this study is attached. (Attachment #7)

Existing IBM practices and procedures will continue to be strictly followed to provide for safe transportation, storage, use, handling, and disposal of TMAH. Adherence to these requirements is verified through routine reviews.

If you should have questions regarding IBM's toxicity testing of TMAH, please contact Dr. Bradford Brooks, IBM Center for Process and Product Toxicology, at (303)924-5621. Please direct all other questions regarding this submission to me.

Sincerely,

Martín-J. Sepúlveda, M.D.
Vice President

MJS/ch
cc: Bradford O. Brooks, Ph.D.
Attachments (7)
By Airborne

(1)

IIT RESEARCH INSTITUTE

Life Sciences

IITRI Project No. 1052/SN1
August 9, 1999

Bradford O. Brooks, Ph.D.
IBM Corporation
P.O. Box 1800
Boulder, CO 80301-9191

Dear Dr. Brooks:

This letter will serve as an amended final report summarizing the data from a Four-Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Sprague-Dawley Rats (i.e.; IITRI Project No. 1052, Study No. 1). The preliminary report submitted March 11, 1999 is amended to correct and clarify items in the previous report and to include the Quality Assurance Statement.

Study Design:

The study was designed to determine the toxicity of graded concentrations of TMAH when applied repeatedly to the shaved dorsal skin. A vehicle control group of equal size was exposed dermally to the vehicle (distilled water) only. Initially, the study was composed of 5 groups consisting of 10 rats/sex/group. However, as described in detail below, the groups of male and female rats were dosed with different graded concentrations of the test substance ultimately resulting in a total of 7 treatment groups between both sexes. The dosing was staggered over two days, with each sex (males and females) being initiated over two consecutive days. The vehicle and test substance formulation was applied to the reservoir of a Hill Top Chamber® (Hill Top Biolabs, Inc., Cincinnati, Ohio) which was then placed on the shaved animal's back behind the shoulder blades. The chamber was held secure with an elastic cloth band fastened with Velcro®. The chamber and wrapping were removed 6 hours after dosing. To prevent potential ingestion of the test substance formulation, each animal was fitted with a plastic neck collar (Ejay International Inc., Glendora, CA) on days of treatment (i.e., collar removed on Saturday morning and replaced on Monday prior to dosing). The rats were weighed prior to treatment initiation (Day 0) of the study and weekly thereafter. Dosing volumes were based on the most current body weight. Food consumption was monitored to coincide with body weights. Rats were observed daily for overt signs of toxicity. At least once per week rats were given a thorough hand-held clinical examination which included evaluation of the application site skin.

The initial target dose levels were 0, 0.55, 5, 12 and 25% w/v. The dosages were administered 6 hours/day, 5 days/week, at a constant volume of 1 ml/kg. These dose levels were equivalent to 0, 5.5, 50, 120 and 250 mg/kg/day. On the first day of administration all male rats in the 120 and 250 mg/kg groups died within 3 hours of administration and one male in the 50 mg/kg group died. As a result of these deaths, the dose levels to be administered to the female rats were lowered.

Therefore, a total of 7 treatment groups (a vehicle control and 6 TMAH dose levels) were evaluated between both sexes. The study dose levels were as follows:

Males		Females	
Dose Level (%)	Dosage (mg/kg)	Dose Level (%)	Dosage (mg/kg)
0	0	0	0
0.55	5.5	0.25	2.5
5	50	0.55	5.5
12	120	1	10
25	250	5	50

Because of the early deaths, other design changes were implemented. In an attempt to determine a possible cause of test substance induced toxicity/moribundity, blood samples were collected via the retroorbital plexus from five male and five female rats in the 5% dose level group for hematology and limited serum chemistry analysis on study days 4 and 3, respectively. In addition, rats dying spontaneously within the first week of the study were subjected to a gross necropsy and any tissues with grossly observable lesions (excluding application site skin) were collected. After one week of treatment the rats that died (five in the 50 mg/kg dose group) were subjected to a complete necropsy and their tissues were preserved, regardless of gross appearance. At study termination (day 29) all surviving rats were euthanized, a gross necropsy performed and all gross lesions were collected and preserved in 10% neutral buffered formalin for possible microscopic evaluation.

Results:

All of the male rats in the 120 and 250 mg/kg dose groups died within 3 hours of treatment initiation. Clinical signs noted in these groups were lethargy followed by convulsions, tremors, and death beginning within 1-1/2 to 2 hours after administration of the first dose of TMAH. Conversely, no overt signs of systemic toxicity were observed in the 50 mg/kg males although one male died on the first day of treatment. The remaining 50 mg/kg male and female rats died intermittently throughout the study with the longest survival being approximately 2 weeks. One female rat in the 50 mg/kg dose group exhibited hypoactivity and labored breathing. No deaths and no overt clinical signs of toxicity were observed at the lower doses (males, 5.5 mg/kg; females, 2.5, 5.5, or 10 mg/kg).

Application site skin irritation included erythema, edema and/or scabbing in all groups treated with the test substance (Table 1). Some of the scabbing (i.e.; possible grooming irritation) may be associated with the animal's instinctive grooming behavior occurring when the collars were removed on the weekends. Besides irritation at the application site skin, no gross lesions were noted in any of the 120 or 250 mg/kg dose group rats that died. Gross lesions, other than application site lesions, were noted in four 50 mg/kg treatment group rats and included red lungs (3 rats), urinary bladder calculus (2 rats), red ovaries (2 rats), dark eye (1 rat) and small seminal vesicles (1 rat). Red ovaries were also observed in all surviving rats at the 10 mg/kg (10/10) and 4/10 at the 5.5 mg/kg dose levels.

Body weight gain was significantly reduced in the 4 surviving high dose females at week 1. No other significant differences were seen in body weights (Table 2), body weight gains (Table 3) or food consumption (Table 4). No overt changes in blood hematology (Tables 5 and 7) or chemistry were seen, with the possible exception of a moderate increase in alkaline phosphatase was noted in the male rats in the 50 mg/kg group (Table 6).

John Findlay 8/9/99

John Findlay, B.S. Date
Study Director
Life Sciences Operation

Bernadette Ryan 8/9/99

Bernadette Ryan, Ph.D., D.A.B.T. Date
Study Toxicologist
Manager, Regulatory Toxicology Division
Life Sciences Operation

QUALITY ASSURANCE STATEMENT

Study Title:	Four Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats
Project Number:	1052
Study Number:	1
Study Director:	John Findlay, B.S.

This study has been inspected and this amended report was audited by the IITRI Quality Assurance Unit. The reported results accurately reflect the raw data of the study.

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

Date of Inspection	Findings Reported to: Study Director	Management
January 12-13, 1999	January 13, 1999	May 4, 1999
January 28, 1999	May 4, 1999	May 4, 1999
February 1, 1999	May 4, 1999	May 4, 1999
February 2, 1999	May 4, 1999	May 4, 1999
February 3, 1999	February 3, 1999	February 5, 1999
February 8, 1999	May 4, 1999	May 4, 1999
March 1, 1999	May 4, 1999	May 4, 1999
March 2, 1999	May 4, 1999	May 4, 1999
March 29, 1999	March 29, 1999	April 19, 1999
April 14-15, 1999	April 15, 1999	April 19, 1999
April 29-30, May 3-4, 1999	May 4, 1999	August 6, 1999
May 6, 1999	August 6, 1999	August 6, 1999
August 4-5, 1999	August 5, 1999	August 9, 1999
August 6, 1999	August 6, 1999	August 6, 1999
August 6, 1999	August 9, 1999	August 9, 1999

R. A. Boyne 8-9-99

Ronald A. Boyne, B.S. Date
Manager, Quality Assurance

TABLE 1

SUMMARY OF OBSERVATION FREQUENCY

STUDY: 1052SN1 SEX: MALE

DOSE:(mg/kg)	0	5.5	50	120	250
GROUP:	1-M	2-M	3-M	4-M	5-M
Animal found dead	0	0	10	10	10
Normal	10	10	10	10	10
Lesion - scabbed	0	3	4	0	0
Application site-redness	0	0	5	0	0
Application site-edema	0	0	3	0	0
Poss. grooming irritation	0	8	0	0	0
Total Number of Animals	10	10	10	10	10

Poss. = Possible

Incidence reflects the number of animals that exhibited the sign at some time during the study including one day prior to dosing.

Due to the rapidity of deaths (i.e. within 3 hours of dosing) in the male 120 and 250 mg/kg groups, time did not permit the electronic capture of clinical toxicity signs and application site observations. Clinical signs noted were lethargy followed by tremors and convulsions. In addition, the application site (skin) appeared shiny, red and depilated of hair. A general study note documented these findings.

TABLE 1 (cont.)

SUMMARY OF OBSERVATION FREQUENCY

STUDY: 1052SN1 SEX: FEMALE

DOSE:(mg/kg)	0	2.5	5.5	10	50
GROUP:	1-F	2-F	3-F	4-F	5-F
Animal found dead	0	0	0	0	10
Normal	10	10	10	10	10
Hypoactive	0	0	0	0	1
Labored breathing	0	0	0	0	1
Lesion - scabbed	0	3	3	10	4
Application site-redness	0	0	2	4	8
Application site-edema	0	0	1	0	6
Poss. grooming irritation	1	5	6	0	0
Total Number of Animals	10	10	10	10	10

Poss. = Possible

Incidence reflects the number of animals that exhibited the sign at some time during the study including one day prior to dosing.

TABLE 2

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 1052SN1 SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	5.5 2-M	50 3-M	120 4-M	250 5-M
WEEK 0	MEAN	211	206	210	207	209
	S.D.	15.6	13.3	13.6	14.8	16.8
	N	10	10	10	10	10
WEEK 1	MEAN	248	246	246	--	--
	S.D.	21.1	20.3	20.4	--	--
	N	10	10	5	0	0
WEEK 2	MEAN	295	290	--	--	--
	S.D.	27.2	26.4	--	--	--
	N	10	10	0	0	0
WEEK 3	MEAN	336	328	--	--	--
	S.D.	30.2	29.3	--	--	--
	N	10	10	0	0	0
WEEK 4	MEAN	368	360	--	--	--
	S.D.	35.1	36.0	--	--	--
	N	10	10	0	0	0

Analysis of Variance using DUNNETT'S Procedure

* P less than .05
** P less than .01
-- = Data Unavailable

TABLE 2 (cont.)

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 1052SN1 SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	2.5 2-F	5.5 3-F	10 4-F	50 5-F
WEEK 0	MEAN	169	169	164	169	167
	S.D.	8.6	12.6	10.5	10.4	12.0
	N	10	10	10	10	10
WEEK 1	MEAN	189	186	183	186	172
	S.D.	10.6	12.7	9.3	12.1	13.8
	N	10	10	10	10	4
WEEK 2	MEAN	206	203	203	206	--
	S.D.	12.1	17.2	11.6	17.1	--
	N	10	10	10	10	0
WEEK 3	MEAN	224	221	224	221	--
	S.D.	12.0	18.3	13.4	18.9	--
	N	10	10	10	10	0
WEEK 4	MEAN	237	236	236	237	--
	S.D.	13.6	17.7	16.7	18.0	--
	N	10	10	10	10	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

TABLE 3

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 1052SN1 SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	5.5 2-M	50 3-M	120 4-M	250 5-M
WEEK 1	MEAN	38	40	37	--	--
	S.D.	7.9	9.3	9.8	--	--
	N	10	10	5	0	0
WEEK 2	MEAN	47	44	--	--	--
	S.D.	6.4	7.8	--	--	--
	N	10	10	0	0	0
WEEK 3	MEAN	41	38	--	--	--
	S.D.	5.8	4.9	--	--	--
	N	10	10	0	0	0
WEEK 4	MEAN	33	32	--	--	--
	S.D.	7.9	7.3	--	--	--
	N	10	10	0	0	0
TOTAL GAIN	MEAN	158	154	--	--	--
	S.D.	21.6	24.2	--	--	--
	N	10	10	0	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

TABLE 3 (cont.)

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 1052SN1 SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	2.5 2-F	5.5 3-F	10 4-F	50 5-F
WEEK 1	MEAN	21	17	18	17	8**
	S.D.	4.5	5.6	5.4	4.5	5.4
	N	10	10	10	10	4
WEEK 2	MEAN	17	18	21	20	--
	S.D.	5.8	9.8	4.3	7.3	--
	N	10	10	10	10	0
WEEK 3	MEAN	18	18	20	16	--
	S.D.	4.0	5.9	4.3	5.9	--
	N	10	10	10	10	0
WEEK 4	MEAN	13	15	13	15	--
	S.D.	6.1	4.8	5.2	4.7	--
	N	10	10	10	10	0
TOTAL GAIN	MEAN	68	67	72	68	--
	S.D.	10.9	9.3	11.7	9.2	--
	N	10	10	10	10	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

TABLE 4

SUMMARY OF FOOD CONSUMPTION (Grams)

STUDY: 1052SN1 SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	5.5 2-M	50 3-M	120 4-M	250 5-M
WEEK 1	MEAN	188	185	182	-	-
	S.D.	21.6	13.6	20.2	-	-
	N	10	10	4	0	0
WEEK 2	MEAN	213	205	-	-	-
	S.D.	21.1	20.2	-	-	-
	N	10	10	0	0	0
WEEK 3	MEAN	227	216	-	-	-
	S.D.	22.1	19.8	-	-	-
	N	10	10	0	0	0
WEEK 4	MEAN	229	221	-	-	-
	S.D.	20.4	21.2	-	-	-
	N	10	10	0	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

TABLE 4 (cont.)

SUMMARY OF FOOD CONSUMPTION (Grams)

STUDY: 1052SN1 SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	2.5 2-F	5.5 3-F	10 4-F	50 5-F
WEEK 1	MEAN	155	155	152	155	143
	S.D.	10.8	14.3	9.6	6.8	16.9
	N	10	10	10	10	4
WEEK 2	MEAN	165	164	163	171	-
	S.D.	12.6	13.3	10.1	11.4	-
	N	10	10	10	10	0
WEEK 3	MEAN	171	171	172	176	-
	S.D.	12.2	14.5	11.2	11.3	-
	N	10	10	10	10	0
WEEK 4	MEAN	177	178	175	180	-
	S.D.	14.0	15.2	12.6	10.9	-
	N	10	10	10	10	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

TABLE 5

SUMMARY OF HEMATOLOGY DATA
PERIOD: 02-05-99

SEX:. MALE

STUDY ID: 1052-1

GROUP(s): 50 mg/kg

Test: LEUKOCYTES (thsn/cmm)

MEAN	16.5
SD	3.61
N	5

Test: ERYTHROCYTES (mill/cmm)

MEAN	6.31
SD	0.348
N	5

Test: HEMOGLOBIN (g/dL)

MEAN	14.5
SD	0.76
N	5

Test: HEMATOCRIT (%)

MEAN	41.9
SD	1.92
N	5

Test: MEAN CORPUSCULAR VOLUME (fl)

MEAN	66.5
SD	1.36
N	5

Test: MEAN CORPUSCULAR HEMOGLOBIN (pg)

MEAN	23.0
SD	0.54
N	5

Test: MEAN CORP.HEMOGLOBIN CONC. (%)

MEAN	34.6
SD	0.37
N	5

WBC corrected for NRBC > 0

TABLE 5 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: MALE

GROUP(s): 50 mg/kg

Test: PLATELETS (thsn/cmm)

MEAN	1247
SD	67.6
N	5

Test: RETICULOCYTES(%) (%)

MEAN	4.2
SD	1.17
N	5

Test: RETICULOCYTES (Absolute#) (thsn/cmm)

MEAN	265.3
SD	65.14
N	5

Test: Nucleated Red Cells (#/100 WBC)

MEAN	0.0
SD	0.00
N	5

Test: MAT NEU (thsn/cmm)

MEAN	2.4
SD	0.72
N	5

Test: LYMPH (thsn/cmm)

MEAN	13.5
SD	3.23
N	5

Test: MONO (thsn/cmm)

MEAN	0.4
SD	0.12
N	5

WBC corrected for NRBC > 0

TABLE 5 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1 SEX: MALE

GROUP(s): 50 mg/kg

Test: EOSIN (thsn/cmm)

MEAN	0.2
SD	0.20
N	5

Test: BASO (thsn/cmm)

MEAN	0.0
SD	0.00
N	5

Test: IMM NEU (thsn/cmm)

MEAN	0.0
SD	0.00
N	5

WBC corrected for NRBC > 0

TABLE 5 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: FEMALE

GROUP(s): 50 mg/kg

Test: LEUKOCYTES (thsn/cmm)

MEAN	12.7
SD	1.94
N	4

Test: ERYTHROCYTES (mill/cmm)

MEAN	6.82
SD	0.188
N	4

Test: HEMOGLOBIN (g/dL)

MEAN	15.3
SD	1.12
N	4

Test: HEMATOCRIT (%)

MEAN	43.1
SD	1.66
N	4

Test: MEAN CORPUSCULAR VOLUME (fl)

MEAN	63.1
SD	1.48
N	4

Test: MEAN CORPUSCULAR HEMOGLOBIN (pg)

MEAN	22.5
SD	1.16
N	4

Test: MEAN CORP.HEMOGLOBIN CONC. (%)

MEAN	35.6
SD	1.27
N	4

WBC corrected for NRBC > 0

N = 4 due to sample clotting

TABLE 5 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1 SEX: FEMALE

GROUP(s): 50 mg/kg

Test: PLATELETS (thsn/cmm)	
MEAN	1296
SD	206.1
N	4
Test: RETICULOCYTES(%) (%)	
MEAN	3.6
SD	0.60
N	4
Test: RETICULOCYTES (Absolute#) (thsn/cmm)	
MEAN	241.4
SD	35.83
N	4
Test: Nucleated Red Cells (#/100 WBC)	
MEAN	0.0
SD	0.00
N	4
Test: MAT NEU (thsn/cmm)	
MEAN	1.9
SD	0.48
N	4
Test: LYMPH (thsn/cmm)	
MEAN	10.5
SD	2.17
N	4
Test: MONO (thsn/cmm)	
MEAN	0.3
SD	0.12
N	4

WBC corrected for NRBC > 0

N = 4 due to sample clotting

TABLE 5 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: FEMALE

GROUP(s): 50 mg/kg

Test: EOSIN (thsn/cmm)

MEAN	0.0
SD	0.05
N	4

Test: BASO (thsn/cmm)

MEAN	0.0
SD	0.00
N	4

Test: IMM NEU (thsn/cmm)

MEAN	0.0
SD	0.00
N	4

WBC corrected for NRBC > 0

N = 4 due to sample clotting

TABLE 6

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1 SEX: MALE

GROUP(s): 50 mg/kg

Test: Sodium (mmol/L)	
MEAN	143
SD	0.8
N	5

Test: Potassium (mmol/L)	
MEAN	6.3
SD	0.37
N	5

Test: Chloride (mmol/L)	
MEAN	101
SD	2.5
N	5

Test: Calcium (mg/dL)	
MEAN	10.6
SD	0.17
N	5

Test: Phosphate (Inorganic) (mg/dL)	
MEAN	10.8
SD	0.54
N	5

Test: Creatine Kinase (IU/L)	
MEAN	441
SD	171.9
N	5

Test: Alkaline Phosphatase (IU/L)	
MEAN	367
SD	76.3
N	5

TABLE 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: MALE

GROUP(s): 50 mg/kg

Test: Alanine Aminotransferase (IU/L)

MEAN	43
SD	2.1
N	5

Test: Aspartate Aminotransferase (IU/L)

MEAN	93
SD	19.1
N	5

Test: Total Bilirubin (mg/dL)

MEAN	0.36
SD	0.036
N	5

Test: Blood Urea Nitrogen (mg/dL)

MEAN	13
SD	2.8
N	5

Test: Creatinine (mg/dL)

MEAN	0.4
SD	0.08
N	5

Test: Glucose (mg/dL)

MEAN	123
SD	8.1
N	5

Test: Total Protein (g/dL)

MEAN	5.3
SD	0.25
N	5

TABLE 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: MALE

GROUP(s): 50 mg/kg

Test: Albumin (g/dL)	
MEAN	4.0
SD	0.11
N	5

Test: Globulin (g/dL)	
MEAN	1.3
SD	0.16
N	5

Test: A/G Ratio (-)	
MEAN	3.1
SD	0.32
N	5

TABLE 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: FEMALE

GROUP(s): 50 mg/kg

Test: Sodium (mmol/L)	
MEAN	143
SD	1.9
N	5
Test: Potassium (mmol/L)	
MEAN	6.0
SD	0.59
N	5
Test: Chloride (mmol/L)	
MEAN	103
SD	2.7
N	5
Test: Calcium (mg/dL)	
MEAN	11.1
SD	0.36
N	5
Test: Phosphate (Inorganic) (mg/dL)	
MEAN	10.7
SD	1.92
N	4
Test: Creatine Kinase (IU/L)	
MEAN	327
SD	130.7
N	4
Test: Alkaline Phosphatase (IU/L)	
MEAN	213
SD	30.7
N	5

Quantity not sufficient for some chemistries

TABLE 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: FEMALE

GROUP(s): 50 mg/kg

Test: Alanine Aminotransferase (IU/L)	
MEAN	41
SD	13.3
N	5
Test: Aspartate Aminotransferase (IU/L)	
MEAN	98
SD	21.6
N	5
Test: Total Bilirubin (mg/dL)	
MEAN	0.43
SD	0.053
N	4
Test: Blood Urea Nitrogen (mg/dL)	
MEAN	15
SD	1.7
N	5
Test: Creatinine (mg/dL)	
MEAN	0.4
SD	0.13
N	4
Test: Glucose (mg/dL)	
MEAN	132
SD	31.0
N	4
Test: Total Protein (g/dL)	
MEAN	6.0
SD	0.35
N	5

Quantity not sufficient for some chemistries

TABLE 6 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: 02-05-99

STUDY ID: 1052-1

SEX: FEMALE

GROUP(s): 50 mg/kg

Test: Albumin (g/dL)	
MEAN	4.6
SD	0.36
N	4

Test: Globulin (g/dL)	
MEAN	1.4
SD	0.05
N	4

Test: A/G Ratio (-)	
MEAN	3.4
SD	0.13
N	4

Quantity not sufficient for some chemistries

TABLE 7

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052-1 SEX: MALE

GROUP: 50 mg/kg

Animal ID	02-05-99
282	Polychromasia +; Platelets Adequate and Normal
283	Polychromasia +; Anisocytosis +; Macrocytosis +; Platelets Adequate and Normal
285	Polychromasia ++; Anisocytosis +; Macrocytosis +; Poikilocytosis ++; Platelets Adequate and Normal
286	Polychromasia +; Macrocytosis +; Platelets Adequate and Normal
289	Polychromasia +; Anisocytosis +; Poikilocytosis +; Macrocytosis +; Target Cells +; Platelets Adequate and Normal

TABLE 7 (cont.)

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052-1

GROUP: 50 mg/kg

SEX: FEMALE

Animal ID	02-05-99
331	Polychromasia +; Anisocytosis +; Poikilocytosis +
332	Polychromasia +; Anisocytosis +; Poikilocytosis +; Platelets Adequate and Normal
333	Clotted
335	Polychromasia +; Anisocytosis +; Poikilocytosis +; Platelets Adequate and Normal
340	Polychromasia +; Anisocytosis +; Poikilocytosis +; Platelets Adequate and Normal

BEGIN MSDS 910038180

SECTION 1 CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

MDL INFORMATION SYSTEMS, INC.
1281 Murfreesboro Road, Suite 300
Nashville, TN 37217-2423
1-615-366-2000

EMERGENCY TELEPHONE NUMBER:
1-800-424-9300 (NORTH AMERICA)
1-703-527-3887 (INTERNATIONAL)

SUBSTANCE: TETRAMETHYLAMMONIUM HYDROXIDE, 10-25% (AQUEOUS SOLUTION)

TRADE NAMES/SYNONYMS:
420002314; 420004393; TETRAMETHYLAMMONIUM HYDROXIDE, 25% IN WATER; TETRAMETHYLAMMONIUM HYDROXIDE, 25% (AQUEOUS); METHANAMINIUM, N,N,N-TRIMETHYL, HYDROXIDE; TMH; TMAH; 910038183; 910038186; C4H12N.HO; TETRAMETHYLAMMONIUM HYDROXIDE, 25%; OHSIS727

PRODUCT USE: analytical chemical/laboratory chemical

CREATION DATE: Aug 26 1993
REVISION DATE: Mar 16 1999

SECTION 2 COMPOSITION, INFORMATION ON INGREDIENTS

COMPONENT: TETRAMETHYL AMMONIUM HYDROXIDE
CAS NUMBER: 75-59-2
EC NUMBER (EINECS): 200-882-9
PERCENTAGE: 10-25

COMPONENT: WATER
CAS NUMBER: 7732-18-5
EC NUMBER (EINECS): 231-791-2
PERCENTAGE: 75

SECTION 3 HAZARDS IDENTIFICATION

NFPA RATINGS (SCALE 0-4): HEALTH=4 FIRE=1 REACTIVITY=0

EC CLASSIFICATION (CALCULATED): No classification assigned.

EMERGENCY OVERVIEW:
COLOR: colorless to yellow
PHYSICAL FORM: solution
ODOR: fishy odor
MAJOR HEALTH HAZARDS: potentially fatal on contact with the skin, respiratory tract burns, skin burns, eye burns, mucous membrane burns

POTENTIAL HEALTH EFFECTS:
INHALATION:
SHORT TERM EXPOSURE: burns
LONG TERM EXPOSURE: same as effects reported in short term exposure
SKIN CONTACT:
SHORT TERM EXPOSURE: burns, potentially fatal on contact with the skin
LONG TERM EXPOSURE: same as effects reported in short term exposure
EYE CONTACT:
SHORT TERM EXPOSURE: burns
LONG TERM EXPOSURE: same as effects reported in short term exposure
INGESTION:

SHORT TERM EXPOSURE: burns
LONG TERM EXPOSURE: same as effects reported in short term exposure

CARCINOGEN STATUS:
OSHA: N
NTP: N
IARC: N

SECTION 4 FIRST AID MEASURES

INHALATION: When safe to enter area, remove from exposure. Use a bag valve mask or similar device to perform artificial respiration (rescue breathing) if needed. Keep warm and at rest. Get medical attention immediately.

SKIN CONTACT: Remove contaminated clothing, jewelry, and shoes immediately. Wash with soap or mild detergent and large amounts of water until no evidence of chemical remains (at least 15-20 minutes). For burns, cover affected area securely with sterile, dry, loose-fitting dressing. Get medical attention immediately.

EYE CONTACT: Wash eyes immediately with large amounts of water, occasionally lifting upper and lower lids, until no evidence of chemical remains. Continue irrigating with normal saline until ready to transport to hospital. Cover with sterile bandages. Get medical attention immediately.

INGESTION: Never make an unconscious person vomit or drink fluids. Give water or milk. If vomiting occurs, keep head lower than hips to help prevent aspiration. If person is unconscious, turn head to side. Get medical attention immediately.

NOTE TO PHYSICIAN: For inhalation, consider oxygen. Avoid gastric lavage or emesis.

SECTION 5 FIRE FIGHTING MEASURES

FIRE AND EXPLOSION HAZARDS: Slight fire hazard.

EXTINGUISHING MEDIA: carbon dioxide, regular dry chemical, regular foam, water

FIRE FIGHTING: Move container from fire area if it can be done without risk. Cool containers with water spray until well after the fire is out. Flood with fine water spray. Avoid inhalation of material or combustion by-products. Stay upwind and keep out of low areas.

FLASH POINT: >200 F (>93.3 C) (CC)
FLAMMABILITY CLASS (OSHA): IIIB

HAZARDOUS COMBUSTION PRODUCTS:
Combustion products: oxides of carbon, oxides of nitrogen

SECTION 6 ACCIDENTAL RELEASE MEASURES

OCCUPATIONAL RELEASE:
Do not touch spilled material. Stop leak if possible without personal risk. Reduce vapors with water spray. Small spills: Absorb with sand or other non-combustible material. Collect spilled material in appropriate container for disposal. Keep unnecessary people away, isolate hazard area and deny entry.

SECTION 7 HANDLING AND STORAGE

Store and handle in accordance with all current regulations and standards. Keep separated from incompatible substances. See original container for storage recommendations. Store with bases.

SECTION 8 EXPOSURE CONTROLS, PERSONAL PROTECTION

EXPOSURE LIMITS:
TETRAMETHYLAMMONIUM HYDROXIDE, 10-25% (AQUEOUS SOLUTION):
No occupational exposure limits established.

VENTILATION: Provide local exhaust ventilation system. Ensure compliance with applicable exposure limits.

EYE PROTECTION: Wear splash resistant safety goggles with a faceshield. Provide an emergency eye wash fountain and quick drench shower in the immediate work area.

CLOTHING: Wear appropriate chemical resistant clothing.

GLOVES: Wear appropriate chemical resistant gloves.

PROTECTIVE MATERIAL TYPES: rubber

RESPIRATOR: Under conditions of frequent use or heavy exposure, respiratory protection may be needed. Respiratory protection is ranked in order from minimum to maximum. Consider warning properties before use.
Any chemical cartridge respirator with organic vapor cartridge(s).
Any chemical cartridge respirator with a full facepiece and organic vapor cartridge(s).
Any air-purifying respirator with a full facepiece and an organic vapor canister.
For Unknown Concentrations or Immediately Dangerous to Life or Health -
Any supplied-air respirator with full facepiece and operated in a pressure-demand or other positive-pressure mode in combination with a separate escape supply.
Any self-contained breathing apparatus with a full facepiece.

SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL STATE: liquid
COLOR: colorless to yellow
PHYSICAL FORM: solution
ODOR: fishy odor
BOILING POINT: 216 F (102 C) approximate
FREEZING POINT: Not available
VAPOR PRESSURE: Not available
VAPOR DENSITY: Not available
SPECIFIC GRAVITY (water=1): 1.014 @ 20 C
WATER SOLUBILITY: miscible
PH: >13
VOLATILITY: Not available
ODOR THRESHOLD: Not available
EVAPORATION RATE: Not available
COEFFICIENT OF WATER/OIL DISTRIBUTION: Not available

SECTION 10 STABILITY AND REACTIVITY

REACTIVITY: Stable at normal temperatures and pressure.

CONDITIONS TO AVOID: Avoid heat, flames, sparks and other sources of ignition.
May ignite or explode on contact with combustible materials.

INCOMPATIBILITIES: acids, oxidizing materials

HAZARDOUS DECOMPOSITION:
Combustion products: oxides of carbon, oxides of nitrogen
Thermal decomposition products: alcohols, amines

POLYMERIZATION: Will not polymerize.

SECTION 11 TOXICOLOGICAL INFORMATION

TETRAMETHYL AMMONIUM HYDROXIDE:
TOXICITY DATA:
25 mg/kg skin-guinea pig LD50
LOCAL EFFECTS:
Corrosive: inhalation, skin, eye, ingestion
ACUTE TOXICITY LEVEL:
Highly Toxic: dermal absorption

SECTION 12 ECOLOGICAL INFORMATION

Not available

SECTION 13 DISPOSAL CONSIDERATIONS

Subject to disposal regulations: U.S. EPA 40 CFR 262. Hazardous Waste
Number(s): D002.

SECTION 14 TRANSPORT INFORMATION

U.S. DOT 49 CFR 172.101. SHIPPING NAME-UN NUMBER; HAZARD CLASS; PACKING GROUP;
LABEL:
Tetramethylammonium hydroxide-UN1835; 8; II; Corrosive

SECTION 15 REGULATORY INFORMATION

U.S. REGULATIONS:
TSCA INVENTORY STATUS: Y

TSCA 12(b) EXPORT NOTIFICATION: Not listed.
CERCLA SECTION 103 (40CFR302.4): N
SARA SECTION 302 (40CFR355.30): N
SARA SECTION 304 (40CFR355.40): N
SARA SECTION 313 (40CFR372.65): N
SARA HAZARD CATEGORIES, SARA SECTIONS 311/312 (40CFR370.21):

ACUTE: Y
CHRONIC: N
FIRE: N
REACTIVE: N
SUDDEN RELEASE: N
OSHA PROCESS SAFETY (29CFR1910.119): N
STATE REGULATIONS:
California Proposition 65: N
EUROPEAN REGULATIONS:
EC NUMBER (EINECS): 200-882-9

SECTION 16 OTHER INFORMATION

MSDS SUMMARY OF CHANGES
SECTION 1 CHEMICAL PRODUCT AND COMPANY IDENTIFICATION
SECTION 2 COMPOSITION, INFORMATION ON INGREDIENTS
SECTION 8 EXPOSURE CONTROLS, PERSONAL PROTECTION

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Attachment # 3

An example of the portion of site specific communication from March 1999 that includes work practice information.

Existing IBM procedures and practices must continue to be strictly followed to provide for the safe transportation, storage, handling, use and disposal of TMAH. Adherence to these procedures and practices will be verified by routine reviewing.

Handling:

The potential for skin or eye contact, inhalation of mist, and ingestion of TMAH must be carefully controlled in all operations. This is accomplished by the institution of engineering controls (e.g., exhaust ventilation, tool/process enclosures and bulk-fill systems) wherever possible. Where there is potential for skin or eye contact, appropriate personal protective equipment (PPE) is required. Manual dispensing or handling of TMAH should be avoided and is permitted only with the approval of IBM Industrial Hygiene. In the event that contact occurs, immediately remove potentially contaminated clothing and flush the exposed area with water for at least 15 minutes and call or have a co-worker immediately call Emergency Control at extension 4-3333. In the event of ingestion of TMAH or inhalation of TMAH mist, call Emergency Control immediately.

Engineering Controls

TMAH-using equipment must be equipped with engineering controls to prevent skin or eye contact and inhalation of mist. Specific controls include, but are not limited to:

-enclosures;
-splash guards;
-interlocks which terminate chemical flow upon leaks or other malfunctions;
-liquid leak detection and spill containment; and
-flush, rinse and drain capability.

Emergency Equipment

Drench showers and emergency eye washes are located in the vicinity of TMAH-using operations. Such equipment is positioned to permit access within approximately 10 seconds of any skin or eye contact.

Personal Protective Equipment (PPE):

Consult the table below for the required PPE.

Where there is the potential for splashing of TMAH, the use of chemical goggles, a face shield, a chemical-resistant coat apron, and Ansell Edmont Solvex or MAPA Pioneer Trionic gloves is required. The above items must be appropriately sized so as to eliminate skin and eye contact.

Where there is the potential for foot contact due to splash or liquid release of TMAH, chemical resistant boots must be worn in addition to the above-listed apparel.

All departments must state the specific PPE to be worn in applicable Department Safety Procedures, PPE Hazard Assessments, Manufacturing Process Specifications and Maintenance Procedures. Manufacturing areas must also post in the immediate vicinity of all TMAH-using equipment, conspicuous signs and/or chemical labels, as appropriate, indicating the specific PPE to be used.

Global Occupational Health Services (Medical, Safety Engineering and Industrial Hygiene) and line management have conducted reviews of TMAH-using processes at IBM East Fishkill to assure that proper procedures are being followed. Reviews will continue. If you have any questions regarding TMAH or this memo, contact your building Industrial Hygienist or Occupational Health Services (Medical). The contacts list may be found by following the links to Safety on the East Fishkill web site, by typing SAFETY on a VM command line or by calling 2-SAFE.

Attachment # 3

Personal Protective Equipment Requirements for TMAH-using tasks

Task	Eye Protection	Hand	Body	Foot Protection
Pouring	Chemical Goggles and Face Shield (if behind a hood sash, face shield can be eliminated)	Solvex or Trionic gloves	Chemical resistant Coat apron	Chemical resistant boots (unless waived by Industrial Hygiene)
Maintenance where accidental contact could occur	Chemical Goggles and face shield	Solvex or Trionic gloves	Chemical resistant Coat apron	N/A
Maintenance after drain, flush and pH reduced to 6-9	Chemical Goggles	Solvex or Trionic gloves	As needed (contact Industrial Hygiene for guidance	N/A
Installing and removing dip tubes in drums	Chemical Goggles and face shield	Solvex or Trionic gloves	Chemical resistant Coat apron	N/A
Operations wilh the potential for foot contact	Chemical Goggles and face shield	Solvex or Trionic gloves	Chemical resistant Coat apron	Chemical resistant boots

Emergency Procedures

Emergency Control Services must be contacted immediately at extension 4-3333 in the event of any spill or leak of TMAH.

[redacted]

Attachment #4

Concurrent with the March 1999 TSCA 8(e) notification, we provided the following TMAH suppliers with a summary of IBM's toxicity testing results.

Ashland Chemical
Air Products
Clariant
DuPont
EKC Technologies
Microsi, Inc.
Moses Lake Industries
Nacalai Tesque
Ohka America, Inc.
Olin Microelectronics Materials
Pacific Pac Inc.
Sachem
Shipley
Sotrchem
Tokyo Ohka Kogyo

5

IBM Corp

IBM Corp
Dept G4Y/282 - 3A
5600 Cottle Road
San Jose, CA 95193

Phone: (408) 256-3401
FAX: (408) 256-7448
email: adburrel@us.ibm.com

Monday, March 1, 1999

Miller Nelson Research Inc.,
8 Harris Court, Suite C4,
Monterey, CA 93940

Dear Sirs,
Please find enclosed three (3) different types of gloves labelled A, B, and C.

A = Nitrilite (off white)
B = Solvex (green)
C = Trionic (yellow)

We would like to have permeation studies performed on these three glove samples using the sample, "Green Gel" which has already been shipped to you. I understand that you will be using a standard ASTM methodology. The green gel sample is approximately 50% tetramethyl ammonium hydroxide and an MSDS for this compound should have been shipped with the sample. As stated in an earlier telephone conversation, TMAH has been shown to be lethal in experimental animals via the dermal route and we suggest that you handle it appropriately. Solvex and Trionic gloves were found to provide adequate protection against a 25% solution in water. Please call me if you have any questions.

I have submitted a purchase order requisition today and I will ask the purchasing department to call you with the number.

Sincerely,

A O Burrell

Ann Burrell
Advisory Toxicologist
tel (408) 256-3401
fax (408) 256-7448

copy for files

03/05/99

Miller Nelson Research Inc

PERMEATION TEST REPORT

ASTM F 739-96 (NORMALIZED)

MATERIAL NAME:	NITRILITE	CHALLENGE CHEMICAL:	TETRAMETHYLAM-MONIUM HYDROXIDE
FABRIC LOG OR LOT NO.:	SAMPLE A		
MANUFACTURER:		RUN NO:	PERM23\1218

TEST RESULTS	TEST 1	TEST 2	TEST 3	AVERAGE
NORMALIZED (0.1 UG/SQ CM/MIN) BREAKTHROUGH TIME, MIN	>480	>480	>480	>480
PERMEATION RATE STEADY STATE MAXIMUM, UG/SQ CM/MIN	ND	ND	ND	ND
THICKNESS, MILS	4	4	4	4
WEIGHT, OZ/SQ YD	3.1	3.2	3.2	3.2

TEST DATE:	3-2-99	ANALYTICAL METHOD:	FLAME IONIZATION
PRIOR CONDITIONING:	NONE	COLLECTION SYSTEM:	OPEN LOOP
CAS NO:	75-59-2	COLLECTION MEDIUM VOLUME:	NA
CHEMICAL SOURCE:	IBM CORP	CHEMICAL STATE:	LIQUID
CONCENTRATION:	45.0 %	CHEMICAL CONTACT TYPE	CONTINUOUS
SAMPLING FREQUENCY:	CONTINUOUS	COLLECTION MEDIUM:	AIR
MINIMUM DETECTION LIMIT:	0.15 PPM	POST TEST CONDITON:	NO CHANGE
MINIMUM DETECTABLE RATE:	0.034 UG/SQ CM/MIN		
TEMPERATURE:	25 oC		
TEST DURATION:	8 HOURS		
METHOD MODIFICATION	1 IN. CELL		
SPECIMEN AREA EXPOSED:	5.1 SQ. CM	CLIENT:	IBM CORPORATION
FLOW RATE	300 ML/MIN	CONTACT:	ANN BURRELL

ANALYST _____ 3-5-99
STEPHEN J. PRIANTE DATE

QC _____ 3-5-99
GARY O. NELSON DATE

This data is derived from tests performed in accordance with ASTM F739-96. These tests were performed under laboratory conditions and not under actual usage conditions. Miller-Nelson Research Inc. makes no warranties concerning protection by this material and assumes no liability for use of this material with the chemicals tested. The user should determine the applicability of the conditions when assessing suitability of material for actual anticipated exposure.

Respirator cartridge and permeation testing

Tel 831-647-1551 Fax 831-647-8790
Email gnelson@mbay.net Web www.millernelson.com
8 Harris Court, Suite C-6 Monterey, CA 93940-5713

03/05/99

Miller Nelson Research Inc

PERMEATION TEST REPORT

ASTM F 739-96 (NORMALIZED)

MATERIAL NAME: SOL-VEX
FABRIC LOG OR LOT NO.: SAMPLE B
MANUFACTURER: EDMONT

CHALLENGE CHEMICAL: TETRAMETHYLAMMONIUM HYDROXIDE
RUN NO: PERM23\1219

TEST RESULTS	TEST 1	TEST 2	TEST 3	AVERAGE
NORMALIZED (0.1 UG/SQ CM/MIN) BREAKTHROUGH TIME, MIN	>480	>480	>480	>480
PERMEATION RATE STEADY STATE MAXIMUM, UG/SQ CM/MIN	ND	ND	ND	ND
THICKNESS, MILS	18	18	19	18
WEIGHT, OZ/SQ YD	13.8	13.9	13.9	13.9

TEST DATE: 3-2-99
PRIOR CONDITIONING: NONE
CAS NO: 75-59-2
CHEMICAL SOURCE: IBM CORP
CONCENTRATION: 45.0 %
SAMPLING FREQUENCY: CONTINUOUS
MINIMUM DETECTION LIMIT: 0.15 PPM
MINIMUM DETECTABLE RATE: 0.034 UG/SQ CM/MIN
TEMPERATURE: 25 oC
TEST DURATION: 8 HOURS
METHOD MODIFICATION: 1 IN. CELL
SPECIMEN AREA EXPOSED: 5.1 SQ. CM
FLOW RATE 300 ML/MIN

ANALYTICAL METHOD: FLAME IONIZATION
COLLECTION SYSTEM: OPEN LOOP
COLLECTION MEDIUM VOLUME: NA
CHEMICAL STATE: LIQUID
CHEMICAL CONTACT TYPE CONTINUOUS
COLLECTION MEDIUM: AIR
POST TEST CONDITON: NO CHANGE

CLIENT: IBM CORPORATION
CONTACT: ANN BURRELL

ANALYST Stephen J. Priante 3-5-99
STEPHEN J. PRIANTE DATE

QC Gary O. Nelson 3-5-99
GARY O. NELSON DATE

This data is derived from tests performed in accordance with ASTM F739-96. These tests were performed under laboratory conditions and not under actual usage conditions. Miller-Nelson Research Inc. makes no warranties concerning protection by this material and assumes no liability for use of this material with the chemicals tested. The user should determine the applicability of the conditions when assessing suitability of material for actual anticipated exposure.

Respirator cartridge and permeation testing

Tel 831-647-1551 Fax 831-647-8790
Email gnelson@mbay.net Web www.millernelson.com
8 Harris Court, Suite C-6 Monterey, CA 93940-5713

03/05/99

Miller Nelson Research Inc

PERMEATION TEST REPORT

ASTM F 739-96 (NORMALIZED)

MATERIAL NAME:	TRIONIC	CHALLENGE CHEMICAL:	TETRAMETHYLAM-MONIUM HYDROXIDE
FABRIC LOG OR LOT NO.:	SAMPLE C		
MANUFACTURER:	MAPA PIONEER	RUN NO:	PERM23\1220

TEST RESULTS	TEST 1	TEST 2	TEST 3	AVERAGE
NORMALIZED (0.1 UG/SQ CM/MIN) BREAKTHROUGH TIME, MIN	>480	>480	>480	>480
PERMEATION RATE STEADY STATE MAXIMUM, UG/SQ CM/MIN	ND	ND	ND	ND
THICKNESS, MILS	20	20	20	20
WEIGHT, OZ/SQ YD	14.7	15.0	15.1	14.9

TEST DATE:	3-2-99	ANALYTICAL METHOD:	FLAME IONIZATION
PRIOR CONDITIONING:	NONE	COLLECTION SYSTEM:	OPEN LOOP
CAS NO:	75-59-2	COLLECTION MEDIUM VOLUME:	NA
CHEMICAL SOURCE:	IBM CORP	CHEMICAL STATE:	LIQUID
CONCENTRATION:	45.0 %	CHEMICAL CONTACT TYPE	CONTINUOUS
SAMPLING FREQUENCY:	CONTINUOUS	COLLECTION MEDIUM:	AIR
MINIMUM DETECTION LIMIT:	0.15 PPM	POST TEST CONDITON:	NO CHANGE
MINIMUM DETECTABLE RATE:	0.034 UG/SQ CM/MIN		
TEMPERATURE:	25 oC		
TEST DURATION:	8 HOURS		
METHOD MODIFICATION:	1 IN. CELL		
SPECIMEN AREA EXPOSED:	5.1 SQ. CM	CLIENT:	IBM CORPORATION
FLOW RATE	300 ML/MIN	CONTACT:	ANN BURRELL

ANALYST _____ 3-5-99
STEPHEN J. PRIANTE DATE

QC _____ 3-5-99
GARY O. NELSON DATE

This data is derived from tests performed in accordance with ASTM F739-96. These tests were performed under laboratory conditions and not under actual usage conditions. Miller-Nelson Research Inc. makes no warranties concerning protection by this material and assumes no liability for use of this material with the chemicals tested. The user should determine the applicability of the conditions when assessing suitability of material for actual anticipated exposure.

Respirator cartridge and permeation testing

Tel 831-647-1551 Fax 831-647-8790
Email gnelson@mbay.net Web www.millernelson.com
8 Harris Court, Suite C-6 Monterey, CA 93940-5713

04/29/99

Miller Nelson Research Inc

PERMEATION TEST REPORT

ASTM F 739-96 (NORMALIZED)

MATERIAL NAME:	N-DEX 9905 PFM	CHALLENGE CHEMICAL:	TETRAMETHYLAM-MONIUM HYDROXIDE
FABRIC LOG OR LOT NO.:			
MANUFACTURER:	BEST	RUN NO:	PERM25\1284

TEST RESULTS	TEST 1	TEST 2	TEST 3	AVERAGE
NORMALIZED (0.1 UG/SQ CM/MIN) BREAKTHROUGH TIME, MIN	>480	>480	>480	>480
PERMEATION RATE STEADY STATE MAXIMUM, UG/SQ CM/MIN	ND	ND	ND	ND
THICKNESS, MILS	6	6	6	6
WEIGHT, OZ/SQ YD	4.5	4.4	4.4	4.4

TEST DATE	4-27-99	ANALYTICAL METHOD	FLAME IONIZATION
PRIOR CONDITIONING:	NONE	COLLECTION SYSTEM	OPEN LOOP
CAS NO.	75-59-2	COLLECTION MEDIUM VOLUME.	NA
CHEMICAL SOURCE	IBM CORP	CHEMICAL STATE	LIQUID
CONCENTRATION:	45.0 %	CHEMICAL CONTACT TYPE	CONTINUOUS
SAMPLING FREQUENCY:	CONTINUOUS	COLLECTION MEDIUM	AIR
MINIMUM DETECTION LIMIT	0.15 PPM	POST TEST CONDITON	NO CHANGE
MINIMUM DETECTABLE RATE	0.034 UG/SQ CM/MIN		
TEMPERATURE:	25 oC		
TEST DURATION	8 HOURS		
METHOD MODIFICATION:	1 IN CELL		
SPECIMEN AREA EXPOSED	5 1 SQ. CM	CLIENT:	IBM CORPORATION
FLOW RATE	300 ML/MIN	CONTACT:	ANN BURREL

ANALYST Stephen J. Priante 4-29-99
STEPHEN J. PRIANTE DATE

QC Gary O. Nelson 4-29-99
GARY O. NELSON DATE

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8 Harris Court, Suite C-6 Monterey, CA 93940-5713

08/21/2000 16:02 8316478790 MILLER NELSON RES PAGE 03

04/29/99

Miller Nelson Research Inc

PERMEATION TEST REPORT

ASTM F 739-96 (NORMALIZED)

MATERIAL NAME:	APRON/SMOCK CPP	CHALLENGE CHEMICAL:	TETRAMETHYLAM-MONIUM HYDROXIDE
FABRIC LOG OR LOT NO.:	RN 49636		
MANUFACTURER:	ANSELL EDMONT	RUN NO:	PERM25\1285

TEST RESULTS	TEST 1	TEST 2	TEST 3	AVERAGE
NORMALIZED (0.1 UG/SQ CM/MIN) BREAKTHROUGH TIME, MIN	>480	>480	>480	>480
PERMEATION RATE STEADY STATE MAXIMUM, UG/SQ CM/MIN	ND	ND	ND	ND
THICKNESS, MILS	9	8	9	9
WEIGHT, OZ/SQ YD	7.5	7.4	7.6	7.5

TEST DATE:	4-27-99	ANALYTICAL METHOD	FLAME IONIZATION
PRIOR CONDITIONING.	NONE	COLLECTION SYSTEM.	OPEN LOOP
CAS NO	75-59-2	COLLECTION MEDIUM VOLUME	NA
CHEMICAL SOURCE:	IBM CORP	CHEMICAL STATE:	LIQUID
CONCENTRATION	45.0 %	CHEMICAL CONTACT TYPE	CONTINUOUS
SAMPLING FREQUENCY:	CONTINUOUS	COLLECTION MEDIUM:	AIR
MINIMUM DETECTION LIMIT:	0.15 PPM	POST TEST CONDITON:	NO CHANGE
MINIMUM DETECTABLE RATE:	0.034 UG/SQ CM/MIN		
TEMPERATURE:	25 oC		
TEST DURATION.	8 HOURS		
METHOD MODIFICATION	1 IN CELL		
SPECIMEN AREA EXPOSED:	5.1 SQ. CM	CLIENT:	IBM CORPORATION
FLOW RATE	300 ML/MIN	CONTACT:	ANN BURRELL

ANALYST Stephen J. Priante 4-29-99
STEPHEN J. PRIANTE DATE

QC Gary O. Nelson 4-29-99
GARY O. NELSON DATE

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Email gnelson@mbay.net Web www.millernelson.com
8 Harris Court, Suite C-6 Monterey, CA 93940-5713

Pennline

Fax

Please deliver immediately to:	Ms. Jane Pennline
of:	IBM
Fax number:	1-802-769-4139
Voice number:	
Fax received from:	JOHN E. MACDONALD
of:	MAPA PROFESSIONAL PRODUCTS
Fax number:	(508) 563-5303
Voice number:	(508) 564-5555
Date:	12/2/98
Time:	2:18:53 PM
Number of Pages:	1
Subject:	Trionic E-194 Testing

Message:

Dear Jane,

Here is the information you require on the E-194 Trionic glove. As I explained to you the glove tests excellent for permeation and degradation in the chemical Tetramethylammonium Hydroxide, 75-59-2. If you have any questions or if this doesn't come through well, please give me a call at 1-800-537-2897 vm# 503.
Regards,
John MacDonald
MAPA Professional Products

11/23/98

Miller Nelson Research Inc

PERMEATION TEST REPORT

ASTM F 739-96 (NORMALIZED)

MATERIAL NAME: TRIONIC
FABRIC LOG OR LOT NO: E-194
MANUFACTURER: MAPA PROFESSIONAL

CHALLENGE CHEMICAL: TETRAMETHYLAMMONIUM HYDROXIDE
RUN NO: PERM22\1188

TEST RESULTS	TEST 1	TEST 2	TEST 3	AVERAGE
NORMALIZED (0.1 UG/SQ CM/MIN) BREAKTHROUGH TIME, MIN	>480	>480	>480	>480
PERMEATION RATE STEADY STATE MAXIMUM, UG/SQ CM/MIN	ND	ND	ND	ND
THICKNESS, MILS	20	20	21	20
WEIGHT, OZ/SQ YD	15.1	15.5	15.8	15.4

TEST DATE	11-19-98	ANALYTICAL METHOD	FLAME IONIZATION
PRIOR CONDITIONING	NONE	COLLECTION SYSTEM	OPEN LOOP
CAS NO:	75-59-2	COLLECTION MEDIUM VOLUME	NA
CHEMICAL SOURCE	ALDRICH	CHEMICAL STATE	LIQUID
CONCENTRATION	25 0	CHEMICAL CONTACT TYPE	CONTINUOUS
SAMPLING FREQUENCY	CONTINUOUS	COLLECTION MEDIUM	AIR
MINIMUM DETECTION LIMIT	0.15 PPM	POST TEST CONDITON	NO CHANGE
MINIMUM DETECTABLE RATE	0.034 UG/SQ CM/MIN		
TEMPERATURE	25 oC		
TEST DURATION	8 HOURS		
METHOD MODIFICATION	1 IN CELL		
SPECIMEN AREA EXPOSED	5.1 SQ CM		
FLOW RATE	300 ML/MIN		

ANALYST: STEPHEN J. PRIANTE 11-23-98 DATE

CLIENT: MAPA PROFESSIONAL
CONTACT: RICK MALLERNEE

QC: GARY O. NELSON 11-23-98 DATE

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Miller Nelson Research Inc

PERMEATION TEST REPORT

ASTM F 739-96 (NORMALIZED)

MATERIAL NAME: TRIONIC
FABRIC LOG OR LOT NO: E-184
MANUFACTURER: MAPA PROFESSIONAL

CHALLENGE CHEMICAL: TETRAMETHYLAMMONIUM HYDROXIDE
RUN NO: PERM22\1186

TEST RESULTS	TEST 1	TEST 2	TEST 3	AVERAGE
NORMALIZED (0.1 UG/SQ CM/MIN) BREAKTPROUGH TIME, MIN	>480	>480	>480	>480
PERMEATION RATE STEADY STATE MAXIMUM, UG/SQ CM/MIN	NO	NO	NO	NO
THICKNESS, MILS	20	20	21	20
WEIGHT, OZ/SQ YD	15.1	15.5	15.6	15.4

TEST DATE	11-18-98	ANALYTICAL METHOD:	FLAME IONIZATION
PRIOR CONDITIONING:	NONE	COLLECTION SYSTEM:	OPEN-LOOP
CAS NO:	75-59-2	COLLECTION MEDIUM VOLUME:	NA
CHEMICAL SOURCE:	ALDRICH	CHEMICAL STATE:	LIQUID
CONCENTRATION:	25.0	CHEMICAL CONTACT TYPE	CONTINUOUS
SAMPLING FREQUENCY:	CONTINUOUS	COLLECTION MEDIUM:	AIR
MINIMUM DETECTION LIMIT:	0.13 PPM	POST TEST CONDITON:	NO CHANGE
MINIMUM DETECTABLE RATE	0.034 UG/SQ CM/MIN		
TEMPERATURE:	25 oC		
TEST DURATION:	8 HOURS		
METHOD MODIFICATION:	1 IN CELL		
SPECIMEN AREA EXPOSED:	5.1 SQ. CM		
FLOW RATE	300 ML/MIN		

CLIENT: MAPA PROFESSIONAL
CONTACT: RICK MALLENGEE

ANALYST: STEPHEN J. PRIANTE 11-23-98 DATE

QC: GARY D. NELSON 11-23-98 DATE

This data is derived from tests performed in accordance with ASTM F739-96. These tests were performed under laboratory conditions and not under actual usage conditions. Miller-Nelson Research Inc. makes no warranties concerning protection by this material and assumes no liability for use of this material with the chemicals tested. The user should determine the applicability of the conditions when assessing suitability of material for actual anticipated exposure.

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MAPA *PIONEER*
DEGRADATION TEST REPORT
and
DEGRADATION / PUNCTURE TEST REPORT

Method Standard:	ASTM D471 *	Test Date:	11/19/98
Method Standard:	MAPA-Technical Center-R&D 07. 012. A-10.04.1992	Analyst:	T. Bellac
Glove Style:	Trionic E-194	Test Temperature:	26 C ±2
Material Type:	Triple Polymer Nat,Neo,Nit	Prior Conditioning:	None
Challenge Chemical:	Tetramethylammonium Hydroxide	Concentration:	25%
Chemical Source:	Aldrich	CAS Number:	75 - 59 - 2

****Percent of Weight Gain**

	Cell 1	Cell 2	Cell 3	Average
60 minutes	0.24%	0.17%	0.20%	0.20% - E

0 - 1.0 % Excellent

** The procedure used is for change in mass with liquid on one surface only.

*****Residual Lb. Force** – Puncture test

	Cell 1	Cell 2	Cell 3	Average
Initial Force	6.93 lbs.	7.81 lbs.	8.74 lbs.	7.83 lbs.
60 minutes	8.30 lbs.	5.07 lbs.	7.09 lbs.	6.83 lbs. - E

Before Chemical exposure

After Chemical exposure

Difference in strength of material after exposed to Chemical for period of

*****Percent Degradation**

	Cell 1	Cell 2	Cell 3	Average
60 minutes	19.77 %	35.08 %	18.88 %	24.58 %

7.81 - 5.07 / 7.81

*** The procedure used is set forth in Degradation By Contact With Chemicals Test Method (one sided contact.)

After exposure for period of

Comments: * Test Method has been modified—a 1 5/16" test cell is used and only the 60 minute duration.

Internal test Strength of the material after glove is immersed in ch immersed after the gl has been pun

IBM

INTERNATIONAL BUSINESS MACHINES
1000 RIVER ROAD
ESSEX JUNCION, VT. 05452

FAX # : (802) 769-4139

TO: John Mac Donald

FROM: Jane Pennline

FAX #: 508 - 563 - 5303

PHONE : 802 - 769 - 3321

Fax : 802 - 769 - 4139

PHONE :

SECURITY CLASSIFICATION : UNCLASSIFIED : ✓ CONFIDENTIAL :
INTERNAL USE ONLY :

NUMBER OF PAGES (INCLUDING COVER) : 6

COMMENTS :
John,
Attached, please find the MSDS for the 25% solution of THAH in which we would like the permeation tests to be performed on the Trionic glove. After speaking with our chemical coordinator, the better route (quicker) would be if you could obtain the chemical from the stated manufacturer.
Thank You for your help!

NOTE:
PLEASE DO NOT SEND FACSIMILIES CONTAINING IBM CONFIDENTIAL INFORMATION after 15:30 EST.

TRANMISSIONS TO FOREIGN COUNTRIES OF SOME INFORMATION CONTAINING TECHNICAL DATA IS SUBJECT TO U.S. EXPORT LAW. PLEASE REFERENCE BOP 5-59 OR CONTACT THE BURLINGTON EXPORT REGULATIONS COORDINATOR AT EXTENSION 6-5516 FOR ADDITIONAL INFORMATION.

MID#910038180

RECEIVED
MAR 19 1998

Material Safety Data Sheet

U.S. Format

SUP#42000439
42000234
910038183
910038186

Tetramethylammonium hydroxide, 25% (Aqueous solution)

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Product Number: 707 or 322 or 422 or 494 or 531
Product Name: Tetramethylammonium hydroxide, 25% (Aqueous solution)
Product Synonyms: Methanaminium, N, N, N- trimethyl, hydroxide
or TMH
or TMAH
or C4H12N.HO

Manufacturer:
Sachem, Inc.
2311 Pipeline Road
Cleburne, Texas 76031
USA

Phone: (817) 641-3803

Emergency Telephone Numbers:

Health/Transport	(817) 641-3803	
CHEMTREC	(800) 424-9300	24 Hrs, Everyday

2. COMPOSITION/INFORMATION ON INGREDIENTS

Component	Wt.%	CAS Registry#
Tetramethylammonium hydroxide	25	75-59-2
Water	75	7732-18-5

OSHA HAZARDOUS COMPONENTS (29 CFR1910.1200):

Component	Exposure Limits 8 hrs. TWA (ppm)		
	OSHA PEL	ACGIH TLV	Supplier Rec.
Tetramethylammonium hydroxide Hazard: Corrosive liquid	None Established	None Established	None Established

3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW:
Strongly alkaline liquid. Wear personal protective equipment to prevent contact with eyes and skin. Causes skin burns. Causes respiratory tract and eye irritation. Remove and wash all contaminated clothing before reuse. Thoroughly wash the affected area with water.

POTENTIAL HEALTH EFFECTS:

Inhalation: Very corrosive to mucous membranes, if mists are inhaled. May cause irritation.

Eye Contact: Very corrosive to eyes. May cause irritation.

Skin Contact: Very corrosive to skin. May cause irritation.

Ingestion: Very corrosive.

Chronic: May cause areas of primary irritant dermatitis.

4. FIRST AID MEASURES:

Inhalation: Remove to fresh air. If breathing has stopped, give artificial respiration taking care to avoid contact with this product. Consult a physician.

Eye Contact: IMMEDIATELY flush with water until no evidence of chemical remains (at least 15-20 minutes). Immediately consult a physician.

Skin Contact: Immediately flush with water with sufficient volume until there is no evidence of the chemical on the affected area.

Ingestion: Do not induce vomiting. If person is conscious and able to swallow, have them drink a large volume of water and milk. Immediately contact a physician.

5. FIRE FIGHTING MEASURES:

IGNITION DATA:

Flashpoint: > 200 F Method: Closed Cup
Auto-Ignition Temperature: Not known
Flammable Limits: LEL: N/A UEL: N/A

GENERAL HAZARD:
Corrosive to skin and eyes.

FIRE FIGHTING INSTRUCTIONS:
Avoid splashing onto skin, eyes and clothing. Avoid breathing corrosive vapors.

FIRE FIGHTING EQUIPMENT:
Wear S.C.B.A. May use water spray, carbon dioxide, dry chemical or chemical foam to fight fire.

HAZARDOUS COMBUSTION PRODUCTS:
Emits Carbon monoxide and Nitrogen oxides.

6. ACCIDENTAL RELEASE MEASURES:

LAND SPILL:
Contain spill. If safety allows, stop flow at the source. Prevent contact with skin and clothing. Avoid routing to water bodies or streams. Take up with absorbent material and place in containers for disposal.

WATER SPILL:
Contain spill. If safety allows, stop flow at the source. Prevent contact with skin and clothing. Prevent flow to water supplies. Isolate and take up for disposal.

7. HANDLING AND STORAGE:

STORAGE TEMPERATURE:
May be stored at ambient temperatures. Avoid high temperatures.

STORAGE PRESSURE:
May be stored at ambient pressures.

GENERAL:
Do not get into eyes, on skin or on clothing. Do not breathe mist. Wash all contaminated clothing before reuse. Keep the container tightly closed (readily absorbs carbon dioxide from the air). Should be stored in plastic or stainless steel. Do not eat or drink while handling. Wash thoroughly after handling. Store away from incompatible materials.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION:

ENGINEERING CONTROLS:
Provide controls to prevent splashes and to prevent exposure to mists.

PERSONAL PROTECTIVE EQUIPMENT:
Mist type respirator if exposed to mists. Rubber gloves. Chemical resistant clothing to prevent exposure to skin. Face shield and goggles. Eyewash and safety shower readily available in the immediate area.

9. PHYSICAL AND CHEMICAL PROPERTIES

Vapor Pressure: Not known
Specific Gravity: 1.014 @ 20 C
Solubility in Water: Miscible
pH: >13
Boiling Point: Approx. 102 C
Melting Point: N/A
Viscosity: Not known

Vapor Density*(Air=1)*: Not known
Evap. Rate*(n-Butyl Acetate=1)*: Not known
Freezing Point: Not known
Odor: Amine
Appearance: Colorless to light yellow solution
Physical State: Liquid

10. STABILITY AND REACTIVITY

GENERAL:
Stable at ambient temperatures. Polymerization has never been reported.

INCOMPATIBLE MATERIALS AND CONDITIONS TO AVOID:

Strong acids. Oxidizers should be tested for compatibility before use.
Boiling temperatures should be avoided.

HAZARDOUS DECOMPOSITION:
Trimethylamine and methanol produced during decomposition.
In fire conditions: Carbon monoxide and Nitrogen oxides.

11. TOXICOLOGICAL INFORMATION

Reportedly: Subcutaneous-mouse LDLo = 20 mg/kg (RTECS).
Not identified as an OSHA, NTP or IARC cacinogen. No data available indicating any carcinogenic activity.

12. ECOLOGICAL INFORMATION

If neutralized, this material may be biodegradable. No specific information available.
Acute aquatic toxicity testing on a pH neutralized solution of this compound has been shown to be highly toxic to the ceriodaphnia dubia (water flea).

13. DISPOSAL CONSIDERATIONS

Would be considered as a characteristic waste (DOO2) if disposed in the form as shipped from SACHEM. Incinerate or dispose according to all federal, state and local regulations. Do not discharge directly to surface waters.

14. TRANSPORT INFORMATION

DOT:

PROPER SHIPPING NAME:
Tetramethylammonium hydroxide solution, 8, UN1835, PGII

HAZARD CLASS:
Corrosive

IDENTIFICATION NUMBER:
UN1835

ICAO/IATA:

PROPER SHIPPING NAME:
Tetramethylammonium hydroxide solution, 8, UN1835, PGII

15. REGULATORY INFORMATION

TSCA (Toxic Substance Control Act):
Tetramethylammonium hydroxide is listed on the TSCA Chemical Inventory.

CERCLA (Comprehensive Response Compensation, and Liability Act):
Not listed.

SARA TITLE III (Superfund Amendments and Reauthorization Act):
Not listed. An acute hazard under SARA 311/312.

NOTES: Tetramethylammonium hydroxide is listed on the New Jersey Right To Know Hazardous Substance List.

16. OTHER INFORMATION

NOTES: NIOSH/RTECS (Registry of Toxic Effects of Chemical Substances) Number PA0875000.

Created: 11/08/96
Revised: 08/27/97 by Bryan Hale/SACHEM/US

THE INFORMATION RELATES TO THIS SPECIFIC MATERIAL. IT MAY NOT BE VALID FOR THIS MATERIAL IF USED IN COMBINATION WITH ANY OTHER MATERIALS OR IN ANY PROCESS. IT IS THE USER'S RESPONSIBILITY TO SATISFY ONESELF AS TO THE SUITABILITY AND COMPLETENESS OF THIS INFORMATION FOR HIS OWN PARTICULAR USE.

PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

FINAL REPORT

IITRI Project No.: 1052
Study No.: 2

Testing Facility:

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

Sponsor:

IBM Corporation
P.O. Box 1900
Boulder, CO 80301-9191

Sponsor Representative:
Bradford Brooks, Ph.D.

May 2000

IITRI since 1936 COMMITMENT TO EXCELLENCE

PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

FOREWORD

This report describes a non GLP exploratory dermal toxicity wash study conducted by IIT Research Institute (IITRI) for IBM Corporation. The Sponsor Representative for the study was Bradford Brooks, Ph.D.

John Findlay, B.S., served as Study Director and was responsible for the overall conduct of the study. Mark Kearns, B.S., Laboratory Biologist, was study supervisor and was responsible for the collection of data. Mary Harrington, B.S., Associate Biologist and Raymond Selby, B.S., Laboratory Biologist, also participated in the collection of data for this study. J. Brooks Harder, D.V.M., IITRI staff veterinarian was responsible for animal care. Bartholomew C. Wacek, M.S., Technical Editor, assisted in the preparation of the report.

John Findlay 5/4/00

John Findlay, B.S. Date
Study Director
Life Sciences Operation

PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Study Initiation: May 21, 1999
Experimental Start: May 27, 1999
Experimental Completion: June 11, 1999

SUMMARY

Tetramethylammonium Hydroxide (TMAH; 25%) was applied to the reservoir of a Hill Top Chamber® which was placed behind the animal's shoulder blades and held in direct contact with the intact shaved skin of Sprague-Dawley rats. TMAH was administered at a constant volume of 1 ml/kg of body weight for a specified period of time. The study consisted of 6 groups of TMAH treated rats with each time interval representing a group. The first 5 groups consisted of 3 rats/sex/group and corresponded with exposure to TMAH at durations of 15, 30 or 45 minutes and 1 or 2 hours. The skin was washed with water to remove any residual test substance after the specified exposure time interval. A sixth group consisted of 9 rats/sex/group exposed to TMAH for a duration of 3 hours. This group was further subdivided into three sets of 3 rats/sex. The first set was not washed following test substance exposure. The second set was designated for determination of acetylcholinesterase activity levels in the red blood cells and plasma, and as such, mortality was not measured for these rats. The third and final set was designated for injection of atropine sulfate (atropine sulfate was administered approximately 0.5 hours prior to administration of TMAH and was intended to serve as an antidote control.) A seventh group consisting of 3 rats/sex was exposed to deionized water instead of TMAH and then bled to serve as a vehicle control group for the acetylcholinesterase assay. After the test substance was administered, the rats were observed frequently for overt signs of toxicity and mortality. All rats surviving beyond the first day of treatment were observed once daily for the balance of a 14-day observation period.

All of the rats in the 3-hour exposure group (excluding subset 2) died within 2 hours of TMAH application; including the atropine-injected rats (3/sex). Thus, atropine did not protect the rats from the effects of TMAH. Acetylcholinesterase activity in red blood cells and plasma was unaffected by treatment. Therefore, it is not surprising that atropine sulfate did not alter the response of TMAH exposure. Mortality was observed in 2 of 3 males exposed for 30 minutes and in 3 of the 3 males in the 1- and 2-hour exposure groups. Conversely, mortality was noted in only 1 of 3 females in each of these groups (30-minutes, 1- and 2- hours). All mortalities occurred 1-2 hours after dosing with the exception of one male rat in the 30-minute exposure group that died on day 2. Clinical signs of toxicity noted prior to death consisted of tremors, ptosis, hypoactivity, ataxia, coma, dyspnea and convulsions. All animals in the 15-minute group survived and did not exhibit any overt

signs of toxicity. In addition, no overt signs of toxicity were detected in the surviving female rats in the 30-minute exposure group nor in the one surviving female rat in the 2-hour exposure group. Clinical signs of toxicity as well as mortality appeared to be more pronounced in males than females when the exposure duration was less than 3 hours. Specifically, a total of 8 of 12 males died in the groups exposed to TMAH for 2 hours or less, while in these same groups, only 4 of 12 females died. Application skin of both sexes exhibited signs of dermal irritation consisting of redness, pearl sheen, thickening, eschar and necrosis.

In conclusion, direct contact of TMAH results in severe dermal irritation within as little as 15 minutes and mortality in 30 minutes of contact of the test substance. The adverse effects induced by TMAH (dermal irritation, overt clinical signs of toxicity and the mortality) are directly related to the duration of exposure.

5/4/00

David L. McCormick, Ph.D., D.A.B.T. Date
Vice President and Director
Life Sciences Operation

5/4/00

John Findlay, B.S. Date
Study Director
Life Sciences Operation

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PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

I. INTRODUCTION

The purpose of this study was to determine the dermal toxicity of test substance for various exposure intervals when applied once to the intact skin of rats.

II. MATERIALS AND METHODS

A. Test Substance: TMAH, 25%, (Run No.10806113) was received in a plastic bottle on May 24, 1999. The test substance was a clear liquid and was stored at room temperature (approximately 22°C) protected from light. All chemical analyses and attendant documentation pertaining to the characterization (*e.g.* composition, stability and purity) of the test substance were the responsibility of the Sponsor. The density of the test substance was 1.014 g/ml at 20°C per the Material Safety Data Sheet. The vehicle control group used deionized water.

B. Dosage Formulation: Aliquots of undiluted test substance were dispensed on the day of dosing.

C. Animals: Male and female Sprague-Dawley rats, approximately 5 weeks of age, were purchased from Charles River Laboratories, Portage, MI, for use in this study. The animals were received on May 12, 1999 and a random sample (approximately 15%) of the shipment weighed 76 - 139 g the next day. The rats were held in quarantine for approximately two weeks during which time they were observed daily for survival and at the end of the quarantine period examined carefully to ensure their health and suitability as test subjects. Rats were acclimated to plastic collars by having the collars placed around each animal's neck for approximately 2, 4 and 6 hours on 3 consecutive days, respectively, during the quarantine period. Rats selected for the study were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number.

D. Food and Water: Certified Purina Rodent Chow 5002 (PMI Feeds, Inc., St. Louis, MO) was provided *ad libitum*. City of Chicago municipal water was available *ad libitum* by means of an automatic watering system. No known contaminants were present in the food or water of the animals which would have interfered with the outcome of the study. Reports for the food and water analyses are maintained with facility records.

E. Housing and Environment: The rats were housed individually in suspended stainless steel cages. Absorbent cage liners were placed in the pan below the stainless steel mesh floor of each animal cage to absorb liquids. During the treatment phase of the study, the animal room temperature ranged from 22.0 to 25.5°C and the relative humidity ranged from 27.3 to 64.5%. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness.

F. Methods

1. Experimental Design: Rats used for test substance exposure were selected at random and assigned to five group of three males and three females and one group of nine males and nine females. In addition, a vehicle control (Group 7) for the acetylcholinesterase (AChE) analysis consisted of three males and three females. A summary of the groups is outlined below.

		No. rats/group	
Group	Exposure Time	Male	Female
1	15 min.	3	3
2	30 min.	3	3
3	45 min.	3	3
4	1 hour	3	3
5	2 hour	3	3
6	3 hour	9	9
7	----	3	3

Undiluted TMAH, 25%, was administered dermally at a constant volume of 1 ml/kg body weight for groups 1 through 5. Group 6 was subdivided as follows: 3 rats/sex were exposed to 1 ml/kg body weight of undiluted test substance and not washed, 3 rats/sex were exposed to test substance for approximately 1-2 hours and then bled for AChE, and 3 rats/sex were injected with 10 ml/kg of atropine sulfate just prior to test substance exposure. Group 7 was exposed to deionized water and served as a vehicle control for AChE.

2. Skin Preparation: Approximately 24 hours prior to treatment, fur was clipped between the shoulders (*i.e.*, dorsal scapular region) and the skin examined for abnormalities. Rats found at that time to have significant skin abnormalities were excluded from the study.

3. Dosing: For each group other than the vehicle control, undiluted test substance was dispensed onto a Hill Top Chamber® (Hill Top Biolabs, Inc., Cincinnati, OH)

at a constant dose volume of 1 ml/kg body weight. The chamber was then applied to the clipped shoulder blades of each rat and secured with an elastic band fastened with Velcro®. Each animal was fitted with a plastic neck collar to prevent ingestion or grooming. Wrapping materials and collars were removed at 15-, 30-, 45-minutes and 1-, 2-, and 3-hour intervals after each respective group application. All test sites except those in the 3-hour exposure group were wiped with water-moistened gauze to remove any residual test substance.

4. Clinical Observations: Study animals were observed frequently during treatment and at least once per day for the rest of the 14-day observation period.

5. Body Weights: Study animals were weighed at randomization and on the day of treatment initiation (Day 1).

6. Blood Collection: Blood and plasma samples for acetylcholinesterase (AChE) activity were collected via the retroorbital sinus. Rats were anesthetized (70% CO_2/30% air) approximately 1-2 hours after dosing and prior to death for groups 6 and 7 (3 rats/sex/group).

7. Evaluation of Acetylcholinesterase Activity: At biophase termination, AChE activity was measured in plasma and red blood cells using procedures in Appendix 3. A Beckman CX5 automated clinical chemistry analyzer was used in the assay and data were reported by computerized electronic data capture (LABCAT, IPA, Inc. Princeton, NJ, Version 4.41).

G. Statistics: AChE activity was examined using analysis of variance with post-hoc comparisons made using Dunnett's test. A minimum of $p \leq 0.05$ was used for all comparisons.

H. Deviations: No deviations or circumstances were known to have occurred during the conduct of this study to affect the quality or integrity of the data from this study.

I. Archives: Raw data generated at IITRI during the study and the original final report will be retained in the IITRI archives for five years, at which time the Sponsor will be consulted concerning final disposition of the archival materials.

III. RESULTS

A. Mortality (Table 1): All of the rats in the 3-hour exposure group (excluding subset 2) died within 2 hour of TMAH application including the atropine-injected rats (3/sex). Thus, atropine did not protect the rats from the effects of TMAH. Mortality was

observed in 2 of 3 males exposed for 30 minutes and in 3 of the 3 males in the 1- and 2-hour exposure groups. Conversely, mortality was noted in only 1 of 3 females in each of these groups (30-minutes, 1- and 2- hours). All mortalities occurred 1-2 hours after dosing with the exception of one male rat in the 30-minute exposure group that died on day 2 (i.e., 24 hours following treatment). A total of 8 of 12 males died in the groups exposed to TMAH for 2 hours or less, while in these same groups, only 4 of 12 females died.

B. Clinical Observations (Table 2 and Appendix 1): Clinical signs of toxicity noted shortly after exposure in the 30-and 45-minutes, and 1-, 2-, and 3-hour exposure groups included tremors, ptosis, hypoactivity, ataxia, coma, dyspnea and convulsions. No overt signs of toxicity were observed in any rats in the 15-minute exposure group. In addition, female rats in the 30-minute exposure group as well as one female rat in the 2-hour exposure group showed no overt signs of toxicity. Application skin for all exposure groups exhibited some signs of redness, pearl sheen, thickening, eschar and necrosis.

C. Acetylcholinesterase (AChE) Activity (Table 3 and Appendix 2): AChE activity in plasma and red blood cells was not inhibited compared to the vehicle control.

IV. EVALUATION

Acetylcholinesterase activity was unaffected by treatment, and thus, it is not surprising that atropine did not protect the rats from the effects of TMAH. Clinical signs of toxicity as well as mortality appeared to be more pronounced in males than females when the exposure duration is less than 3 hours. The adverse effects induced by TMAH (dermal irritation, overt clinical signs of toxicity and mortality) are directly related to the duration of exposure with severe skin irritation occurring within as little as 15 minutes and mortality within 30 minutes of contact.

V. TABLES

PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Table 1

Summary of Mortality Data
(3 rats/sex/group)

		Mortality Incidence		
Group	Exposure Time	Males	Females	Combined
1	15 min	0	0	0
2	30 min	2	0	2
3	45 min	0	1	1
4	1 hour	3	1	4
5	2 hour	3	2	5
6	3 hour	3	3	6
6[a]	3 hour	3	3	6

[a] Injected with atropine prior to TMAH exposure

PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Table 2 - Summary of Clinical Observations
(3 rats/sex/group)

	Exposure Period													
	15 min		30 min		45 min		1 hour		2 hour		3 hour		3 hour[a]	
Observations	M	F	M	F	M	F	M	F	M	F	M	F	M	F
No signs observed [b]	3	3	1	3	3	2	--[c]	2	--	1	--	--	--	--
Found dead	--	--	2	--	--	1	3	1	3[d]	2[d]	3[d]	3[d]	3[d]	3[d]
Tremors	--	--	2	--	2	1	2	2	1	--	2	1	2	3
Ptosis	--	--	2	--	1	1	3	2	2	1	3	3	3	3
Hypoactive	--	--	1	--	--	1	2	1	--	--	3	3	2	3
Ataxia	--	--	1	--	--	--	1	1	2	1	2	1	1	3
Coma	--	--	--	--	--	--	1	--	--	--	--	--	--	--
Dyspnea	--	--	1	--	--	--	--	--	--	--	2	1	--	--
Convulsions	--	--	--	--	--	--	--	--	--	1	--	--	--	--
Application Site (Skin)														
Red	2	2	3	3	3	3	3	3	NA	1	NA	NA	NA	NA
Pearl sheen	2	1	3	3	3	3	3	3	NA	1	NA	NA	NA	NA
Eschar	2	1	3	2	3	3	3	3	NA	0	NA	NA	NA	NA
Necrosis	2	1	1	3	3	2	--	2	NA	1	NA	NA	NA	NA
Thickened	--	--	--	--	--	--	3	1	NA	--	NA	NA	NA	NA

[a] Injected with atropine prior to TMAH exposure
[b] Excluding skin irritation
[c] -- = Zero incidence
[d] Died prior to unwrapping and washing - skin not examined

Preliminary Dermal Toxicity Wash Study of Tetramethylammonium Hydroxide (TMAH) in Rats

IITRI Project No. 1052 Study NO. 2

SUMMARY REPORT
PERIOD: Day 1

STUDY ID: 1052SN2 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PCHE(C)	ECHE
UNITS:	U/L	U/L
Group: Group 7M : Vehicle Control		
MEAN	431	3975
SD	76.3	435.9
N	3	3
Group: Group 6M : 3 Hour Exposure		
MEAN	498	3023
SD	214.7	1056.6
N	3	3

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Table 3 (cont.)

Preliminary Dermal Toxicity Wash Study of Tetramethylammonium Hydroxide (TMAH) in Rats

IITRI Project No. 1052 Study NO. 2

SUMMARY REPORT
PERIOD: Day 1

STUDY ID: 1052SN2 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PCHE(C)	ECHE
UNITS:	U/L	U/L
Group: Group 7F : Vehicle Control		
MEAN	689	3650
SD	79.8	109.2
N	3	3
Group: Group 6F : 3 Hour Exposure		
MEAN	757	4200
SD	289.4	415.6
N	3	3

LABCAT CC4.42 16-JUN-1999

VI. APPENDICES

Appendix 1

Individual Clinical Observations
Group 1 (15-min exposure)

Animal Number	Sex	Observation	Study Day Observed
1	M	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
2	M	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
3	M	No signs observed	1-14
4	F	No signs observed	1-14
5	F	No signs observed	2-14
		Red skin	1
6	F	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14

Appendix 1 (cont.)

Individual Clinical Observations
Group 2 (30-min exposure)

Animal Number	Sex	Observation	Study Day Observed
7	M	Animal found dead	2
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Ataxia	1
		Dyspnea	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1
8	M	Animal found dead	1
		Tremors	1
		Ptosis	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1
9	M	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
10	F	No signs observed	14
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-13
11	F	No signs observed	8-14
		Red skin	1
		Pearl sheen to skin	1
		Necrosis	5-7
12	F	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14

Appendix 1 (cont.)

Individual Clinical Observations
Group 3 (45-min exposure)

Animal Number	Sex	Observation	Study Day Observed
13	M	Tremors	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
14	M	Tremors	1
		Ptosis	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
15	M	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
16	F	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
17	F	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
18	F	Animal found dead	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1

PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Appendix 1 (cont.)

Individual Clinical Observations
Group 4 (1-hour exposure)

Animal Number	Sex	Observation	Study Day Observed
19	M	Animal found dead	1
		Tremors	1
		Ptosis	1
		Ataxia	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1
		Thickened skin	1
20	M	Animal found dead	1
		Ptosis	1
		Hypoactive	1
		Coma	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1
		Thickened skin	1
21	M	Animal found dead	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1
		Thickened skin	1

Appendix 1 (cont.)

Individual Clinical Observations
Group 4 (1-hour exposure) [cont.]

Animal Number	Sex	Observation	Study Day Observed
22	F	Red skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14
23	F	Animal found dead	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Red skin	1
		Pearl sheen to skin	1
		Eschar	1
		Thickened skin	1
24	F	Tremors	1
		Ptosis	1
		Ataxia	1
		Red Skin	1
		Pearl sheen to skin	1
		Eschar	1-4
		Necrosis	5-14

Appendix 1 (cont.)

Individual Clinical Observations
Group 5 (2-hour exposure)

Animal Number	Sex	Observation	Study Day Observed
25	M	Animal found dead*	1
26	M	Animal found dead*	1
		Ptosis	1
		Ataxia	1
27	M	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Ataxia	1
28	F	Red skin	1-4
		Pearl sheen to skin	1-4
		Necrosis	5-14
29	F	Animal found dead*	1
30	F	Animal found dead*	1
		Ptosis	1
		Ataxia	1
		Convulsions	1

* Animal died prior to unwrapping and washing

Appendix 1 (cont.)

Individual Clinical Observations
Group 6 (3-hour exposure)

Animal Number	Sex	Observation	Study Day Observed
31	M	Animal found dead*	1
		Ptosis	1
		Hypoactive	1
		Ataxia	1
		Dyspnea	1
32	M	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Dyspnea	1
33	M	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Ataxia	1
40	F	Animal found dead*	1
		Ptosis	1
		Hypoactive	1
		Dyspnea	1
41	F	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
42	F	Animal found dead*	1
		Ptosis	1
		Hypoactive	1
		Ataxia	1

* Animal died prior to unwrapping and washing

Appendix 1 (cont.)

Individual Clinical Observations
Group 6 (3-hour exposure + Atropine)

Animal Number	Sex	Observation	Study Day Observed
37	M	Animal found dead*	1
		Ptosis	1
		Ataxia	1
38	M	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
39	M	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
46	F	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Ataxia	1
47	F	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Ataxia	1
48	F	Animal found dead*	1
		Tremors	1
		Ptosis	1
		Hypoactive	1
		Ataxia	1

* Animal died prior to unwrapping and washing

Preliminary Dermal Toxicity Wash Study of Tetramethylammonium Hydroxide (TMAH) in Rats

IITRI Project No. 1052 Study NO. 2

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: Day 1

STUDY ID: 1052SN2 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Group 7M:Vehicle Control		
49	514	3854
50	364	4459
51	415	3615
MEAN	431	3975
SD	76.3	435.9
N	3	3
GROUP: Group 6M:3 Hour Exposure		
34	251	1807
35	599	3720
36	643	3541
MEAN	498	3023
SD	214.7	1056.6
N	3	3

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Preliminary Dermal Toxicity Wash Study of Tetramethylammonium Hydroxide (TMAH) in Rats

IITRI Project No. 1052 Study NO. 2

INDIVIDUAL ANIMAL REPORT BY GROUP
PERIOD: Day 1

STUDY ID: 1052SN2 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Group 7F:Vehicle Control		
52	778	3643
53	665	3763
54	624	3545
MEAN	689	3650
SD	79.8	109.2
N	3	3
GROUP: Group 6F:3 Hour Exposure		
43	501	3927
44	1071	4678
45	699	3994
MEAN	757	4200
SD	289.4	415.6
N	3	3

LABCAT CC4.42 16-JUN-1999

PRELIMINARY DERMAL TOXICITY WASH STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Appendix 3

Acetylcholinesterase Activity Calculations

Acetylcholinesterase method is a photometric test based on the work of Ellman, *et al.*[1] This method is used on the Beckman CX5 automated clinical chemistry analyzer.

PRINCIPLE

Acetylthiocholine is split into acetate and thiocholine which reacts with dithiobisnitrobenzoic acid (Ellman's reagent) to form the yellow-colored 5-mercapto-2-nitrobenzoic acid. Increasing color intensity is directly proportional to the acetylcholinesterase activity and is measured kinetically at 410 nm.

Acetylthiocholine + cholinesterases → thiocholine + acetate

Thiocholine + dithiobisnitrobenzoic acid → 5-mercapto-2-nitrobenzoic acid

I. COLLECTION

A. Blood: Collected into a 1 ml EDTA tube for the rat (orbital sinus).

II. ASSAY

A. Determine the PCV, SOP CP-730R1 (FOR RAT ONLY)
B. Mix EDTA blood
C. Prepare a 1:10 hemolysate (i.e., 50 μl + 450 μl Ellman's with DI H_2O
D. Centrifuge the remaining blood and remove the plasma
E. Assay both (plasma and hemolysate) for AChE using the CX5 (SOP CP-632R4)
F. Include a tissue blank assay (replace substrate with saline)
G. Use corrected values for calculation of RBC AChE (Substrate U/L - Saline U/L) according to the following:

PCHE = PLASMA AChE
XCHE = PLASMA AChE (blank)
PCHE(C) = PLASMA AChE (CORRECTED) = (PCHE - XCHE)
PCV = HCT
HCHE = HEMOLYSATE AChE
NCHE = HEMOLYSATE AChE (blank)
HCHE(C) = HEMOLYSATE AChE (CORRECTED) X 10 = (HCHE - NCHE) * 10

$$\text{ECHE} = \text{ERYTHROCYTE (RBC) AChE} = \frac{\text{HCHE(C)} - [\text{PCHE(C)} * (1\text{-PCV})]}{\text{PCV}}$$

[1] Ellman, G.L., *et al.*, Biochem. Pharmacol. 7, 1988 (1961).

Appendix 4

IITRI PROJECT NO. 1052
Study No. 2

PROTOCOL

1. Title: Preliminary Dermal Toxicity Wash Study of Tetramethylammonium Hydroxide (TMAH) in Rats

2. Sponsor:
IBM Corporation
P.O. Box 1900
Boulder, CO 80301-9191

3. Testing Facility:
IIT Research Institute
10 West 35th Street
Chicago, IL 60616

4. Objective: The objective of the study is to determine the toxicity for various exposure intervals of the test substance when applied to the intact skin of rats.

5. Duration: The maximum duration of the study will be 3 hours

6. Proposed Study Dates:

a. Treatment Initiation: May 25, 1999
b. Biophase Termination: May 25, 1999
c. Draft Report Completion: June 22, 1999

7. Protocol Approval:

a. Study Director: John Findlay — John Findlay, B.S. — Date: 5/21/99

b. Manager of Research: Bernadette Ryan — Bernadette Ryan, Ph.D., D.A.B.T. — Date: 5/24/99

c. Sponsor Representative: Bradford Brooks — Bradford Brooks, Ph.D. — Date: 5/24/99

8. This protocol complies with specific requirements of the Sponsor.

9. Test Substance:

   a. Identification: The test substance has been identified by the Sponsor as Tetramethylammonium Hydroxide, 25% [(TMAH). Its physical description and batch and/or lot number(s) will be documented in the raw data book. The vehicle for the test substance is DI water.

   b. Assay: Characterization of the bulk test substance is the responsibility of the Sponsor.

   c. Preparation and Storage: The bulk test substance and vehicle will be stored at room temperature (approximately 22°C) protected from light.

   d. Handling Precautions: When working with the test substance, personnel should wear eye protection, dust/mist respirator, tyvek sleeves, apron, and two pairs of gloves (latex over polyethylene).

   e. Test Substance Disposition: Reserve samples will be retained by the Sponsor. At the time of study termination, arrangements will be made for the return of any residual test substance and vehicle to the Sponsor. IITRI will not be required to retain any samples.

   f. Route of Administration: Dermal application.

10. Test System:

   a. Model: Twenty-seven male and 27 female Sprague-Dawley rats (Charles River Laboratories, Portage, MI) will be used in this study. Rats will be approximately 4-5 weeks old and weigh approximately 75 to 100 grams upon arrival from the supplier, and will be approximately 6-8 weeks of age at the time of treatment initiation.

   b. Justification for Selection: The Sprague-Dawley rat is a model widely used for toxicity testing. A significant body of experience with this animal exists against which its reaction to the test substance can be evaluated, and it meets the requirements of relevant test standards.

   c. Housing: Rats will be single-housed in suspended stainless steel wire cages (approximately 25 x 18 x 18 cm) during the study.

   d. Cleaning and Sanitation: Animal rooms and cages will be cleaned and sanitized prior to housing animals in them. Cages and racks will be cleaned, sanitized and changed every two weeks. The changing of cages and racks will be documented in the study notebook. Absorbent animal cage boards will be placed in the dropping trays under the suspended cages and will be replaced at intervals of no more than four days.

e. Food: Certified Purina Rodent Chow #5002 (PMI Feeds Inc., St. Louis MO) will be provided **ad libitum** except during scheduled fasting periods. Manufacturer's analytical results from the lot(s) of diet used in the study will be maintained in a central file at IITRI. To the best of our knowledge no known contaminants are expected to be present in the diet that would interfere with the test substance or test system and would confound the interpretation of the study.

f. Water: City of Chicago water will be provided **ad libitum** by means of an automatic animal watering system. The water is periodically monitored for bacterial contamination and chemical composition (electrolytes, metals, etc.); the results of this monitoring are maintained in a central file at IITRI. There are no known levels of contaminants in the drinking water that will adversely impact the integrity of the study.

g. Animal Identification: Temporary identification numbers will be assigned to the animals prior to randomization. A permanent number will be assigned to each animal following randomization. Each animal will have a permanent numerical identifier marked on its tail which is unique within the study. The animal and study numbers will be displayed on individual cage cards.

h. Environmental Control: Animal rooms will be lighted with fluorescent lights and maintained on a 12-hour light/12-hour dark cycle. Room temperature and humidity readings will be recorded daily and regulated to avoid extreme fluctuations.

11. Experimental Design:

The study will be composed of 5 groups consisting of 3 rats/sex/group undiluted TMAH, 25%, whereas a sixth group will consist of 9 rats/sex/group. The undiluted TMAH, 25% will be administered dermally, at a constant volume of 1 ml/kg, for 15-, 30- and 45 minutes and 1-, 2- and 3-hour intervals. The application site will be washed with water to remove residual test substance at the end of each exposure interval. In group 6, 3 rats/sex will be exposed 3 hours and not washed, 3 rats/sex will be bled for acetylcholinesterase (AChE) and the remaining 3 rats/sex will be injected with atropine sulfate. Group 7 also consists of 3 rats/sex and will serve as a vehicle control for the AChE analysis. Prior to administration of the first dose, the dorsal skin of the rats will be clipped clean of fur. The test substance formulation will be applied to the reservoir of a Hill Top Chamber® (Hill Top Biolabs, Inc., Cincinnati, Ohio) which will be placed behind the animal's shoulder blades and secured with an elastic band fastened with Velcro®. In order to prevent any potential ingestion of the test substance formulation, each animal will be fitted with a plastic neck collar. The study design is outlined below:

Group	Exposure Time	No. rats/group (♂)	No. rats/group (♀)
1	15 min	3	3
2	30 min	3	3
3	45 min	3	3
4	1 hour	3	3
5	2 hours	3	3
6	3 hours	9	9
7 (ChE Control)	-	3	3

12. Method:

a. Quarantine: The rats purchased for use in this study will be held in quarantine for at least 10 days prior to treatment initiation. Rats will be acclimated to the plastic collars by placing the collars around each animal's neck for a period of approximately 6 hours on at least 3 days during the quarantine period.

b. Selection of Subjects: Each rat will be shaved, weighed and will receive a thorough physical examination to ensure its suitability for use as a test animal. Suitability will be based upon the animal's health status and body weight. The rats used on-test will be selected randomly from a pool of suitable animals.

c. Skin Preparation: Rats will be clipped clean of fur between the shoulders (*i.e.*, dorsal scapular region) prior to randomization. Fur will be clipped prior to test substance administration. Any mechanical trauma to the skin resulting from shaving will be noted in the study record.

d. Test substance Application: Graded concentrations of the test substance, will be applied via the Hill Top Chamber® to the skin on the back of each rat. A dosing volume of 1 ml/kg will be used. The Hill Top Chamber® will be held in place with an elastic band secured with Velcro®. The chamber will be removed 6 hours after dosing. A collar will be placed around the neck of the animal to prevent grooming.

e. Removal: All wrappings and collar will be removed from the animal at 15-, 30- and 45- minutes and 1-, 2- and 3- hour intervals. The application site will be rinsed with Milli-Q water-moistened gauze to remove residual test substance.

f. Injured or Diseased Animals: Animals on test will not be treated for any disease or injury. A complete record of the circumstances and disposition of affected animals will be made in the study notebook.

13. Observations:

a. Moribundity and Mortality: All rats will be observed at least once each day prior to the initiation of treatment and during the treatment period. Dead animals will be removed immediately and discarded without necropsy. The death will be documented in the study notebook.

b. Toxicity: Rats will be observed for signs of overt toxicity during the treatment interval. All overt clinical signs of toxicity will be documented.

c. Physical Examination: A complete physical examination will be performed prior to treatment initiation and the results used for test animal selection.

d. Body Weight: Each rat will be weighed during quarantine for randomization purposes and on the day of treatment initiation (day 1).

14. Acetylcholinesterase Inhibition: Blood samples for AChE will be collected prior to death (or approximately 1-2 hours after dosing) for groups 6 and 7 (3 rats/sex/group).

15. Atropine: Just prior to dosing the 3-hour interval animals, 3 rats/sex will be injected subcutaneous with 10 mg/kg of atropine sulfate.

16. Statistical Analysis: AChE activity will be performed using analysis of variance, with post-hoc comparisons made using Dunnett's test. A minimum significance level of $p \leq 0.05$ will be used for all comparisons.

17. Raw Data Notebooks:

    a. Contents: All original data will be maintained in study notebooks. These will include but not necessarily be limited to the following:

        (1) The original signed protocol with any protocol amendments/deviations.
        (2) Test substance characterization and preparation records.
        (3) Animal purchasing and receiving records and randomization procedures.
        (4) Body weights.
        (5) Daily moribundity/mortality records.
        (7) Observations.
        (8) Physical examinations.
        (9) AChE assay data.

    b. Storage: All original data (*i.e.*, data generated at IITRI), specimens and a copy of the final report will be retained in the IITRI archives for 5 years after the submission of the signed final report. At that time, the Sponsor will be contacted in order to determine the final disposition of the archival materials and will be responsible for all costs associated with continued storage of the archival materials in the IITRI archives or for the shipment of these materials to a new storage facility. IITRI's Quality Assurance Unit will maintain a complete record of the disposition of all archival materials.

18. Personnel: Curriculum vitae for all personnel involved in the execution of the study are on file at IITRI.

19. Final Reports: A copy of a draft letter report summarizing the data will be submitted to the Sponsor for review. After receipt and review of the Sponsor's comments, appropriate changes will be made and two copies of the signed letter report will be provided to the Sponsor.

(7)

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

FINAL REPORT

IITRI Project No.: 1052
Study No.: 3

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May 2000

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Study Initiation: May 21, 1999
Experimental Start: May 25, 1999
Experimental Completion: June 23, 1999

FOREWORD

This report describes a four-week dermal toxicity study conducted by the Life Sciences Operation, IIT Research Institute (IITRI) for IBM Corporation. The study was performed under IITRI Project No. 1052 SN3. The Sponsor Representative for the study was Bradford Brooks, Ph.D.

John Findlay, B.S., served as Study Director and was responsible for the overall conduct of the study. Bernadette Ryan, Ph.D., D.A.B.T., served as Study Toxicologist. Mark Kearns, B.S., Laboratory Toxicologist, was study supervisor and was responsible for the collection of data. Mary Harrington, B.S., Associate Biologist and Raymond Selby, B.S., Laboratory Biologist, also participated in the collection of data for this study. J. Brooks Harder, D.V.M., IITRI staff veterinarian was responsible for animal care. William M. Mega, B.S., Research Biologist/Technical Editor, assisted in the preparation of the report.

Respectfully submitted:

John Findlay 5/8/00

John Findlay, B.S. Date
Study Director
Life Sciences Operation

Approved by:

5/8/00

David L. McCormick, Ph.D., D.A.B.T. Date
Vice President and Director
Life Sciences Operation

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

GLP STATEMENT

This study was conducted in accordance with U.S. EPA Good Laboratory Practice Standards (40 CFR Part 792). The Sponsor was responsible for the characterization and attendant documentation of the bulk test substance. The bulk positive control substance was a purchased material and was characterized by its labeling. The data have been reviewed by the Study Director, who certifies that the information contained in this report is consistent with and supported by the study data and represents an appropriate and accurate conclusion within the context of the study design and evaluation criteria.

John Findlay 5/8/00

John Findlay, B.S. Date
Study Director
Life Sciences Operation

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

SUMMARY

Tetramethylammonium Hydroxide (TMAH) was applied to the shaved skin of Sprague-Dawley rats using a Hill Top Chamber placed behind the animal's shoulder blades and held in direct contact with the skin. The study consisted of seven groups of rats, a vehicle control group treated with deionized (DI) water, five TMAH-treated groups receiving 0.25%, 0.55%, 1%, 3% or 5% (w/w) of TMAH in DI water and a positive control group treated with 5% sodium hydroxide, (NaOH) in DI water (w/w). TMAH formulations and the vehicle control substance were administered at a constant volume of 1 ml/kg of body weight for six hours/day, five days/week for four weeks. The positive control formulation was similarly administered, except the rats were treated for only two (female) or three (male) days prior to being euthanized and disposed without necropsy due to the corrosiveness of the dosing formulation. The following parameters were observed or measured: clinical observations, body weight, body weight gain, food consumption, hematology, clinical chemistry and urinalysis parameters, necropsy, organ weights, microscopic examination of target tissues, and acetylcholinesterase (AChE) activity.

In an effort to further elucidate the overt toxicity induced by TMAH, additional groups of rats were treated and used for blood gas analysis and hematology profiles. Six rats/sex/group were similarly exposed to 0% or 5% (w/w) TMAH in DI water or eight rats/sex were exposed to 25% TMAH for approximately 1-4 hours prior to being anesthetized for blood collection to measure blood gas and hematology parameters.

All of the rats in the 5% TMAH group died within the first three days (except for one male and one female that died on Day 8). Mortality was also observed in 8 of 10 male and 8 of 10 female rats treated with 3% TMAH; these deaths occurred between 1 and 14 days of treatment initiation. Clinical signs of toxicity noted prior to death consisted of tremors, ptosis, hypoactivity, ataxia, dyspnea and convulsions. None of the rats in the 0.25, 0.55 and 1% dose groups died and no overt signs of toxicity were observed. However, application skin from these dose group animals (except the 0.25% TMAH-treated group) exhibited signs of dermal irritation (blanched, scabbed, eschar).

A significant decrease in pH and an increase in PCO_2 were observed in both male and female rats treated with 25% TMAH. In addition, the 25% treated males also had decreased HCO_3, while rats in the 5% TMAH group only had decreased PO_2 levels. The alteration in blood gas profiles indicates that TMAH is causing an acid-base disturbance. This disturbance is likely the primary cause of the deaths noted in the 3 and 5% groups.

No toxicologically significant effects were noted on body weight, body weight gain, organ weights, food consumption, hematology, urinalysis and AChE activity. Test substance-related histopathological changes were observed in the application site skin, lung, thymus and liver. The application skin lesions consisted of necrosis, squamous epithelial hyperplasia, exudative scabs and inflammation, while vacuolation (males), eosinophilic intraplasmic material (males and females) and individual hepatocyte necrosis (males) were considered to be treated-related effects in the liver. Pulmonary congestion associated with pulmonary compromise was noted in the 3% rats which died, while thymic lymphoid necrosis was also noted in the 3% group and was attributed to stress.

Accordingly, dermal application of TMAH for 6 hours/day, 5 day/week for four weeks at dose levels of 0.25%, 0.55%, 1%, 3% and 5% resulted in lethality at 3 and 5% as early as day 1, an acid base disturbance indicated by decreased blood PO_2, decreased blood pH and decreased HCO_3 and an increase in PCO_2 levels. In conclusion, based on the results of this study, the no adverse effect level for systemic toxicity is 1% (10 mg/kg), while for dermal irritation it is 0.55% (5.5 mg/kg) and 0.25% (2.5 mg/kg) in males and females, respectively.

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FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

I. INTRODUCTION

The purpose of this study was to determine the dermal toxicity of TMAH, when applied to the intact skin of rats five days per week for four weeks at various exposure levels.

II. MATERIALS AND METHODS

Table 1 lists abbreviations used in this report and their definitions. The study protocol and protocol amendments are included as Appendix A.

A. Test and Control Substances: Tetramethylammonium hydroxide (TMAH), 25%, (Run No.10806113) was received in a plastic bottle on May 24, 1999. The test substance was a clear liquid and was stored at room temperature (approximately 22 °C) protected from light. All chemical analyses and attendant documentation pertaining to the characterization (*e.g.* composition, stability and purity) of the test substance were the responsibility of the Sponsor. The density of the test substance was 1.014 g/ml at 20 °C per the Material Safety Data Sheet. The positive control substance, sodium hydroxide, NaOH (50 wt% solution in water, Lot B0074500, Acros Organics, Somerville, NJ) was a purchased material and was characterized by its labeling. Dosing formulations were prepared in a vehicle of purified (ASTM 1) distilled water. The vehicle was obtained from an in-house water purification system consisting of a constant recirculating loop comprised of a water softener, a reverse osmosis unit, in-line activated carbon module, deionizing resin beds, in-line germicidal UV lamps and a Millipore Milli-Q® module.

B. Dosage Formulation: The test substance formulations were administered dermally at a constant dosing volume of 1 ml/kg of body weight for all dose levels and were prepared in Milli-Q water at 0.25, 0.55, 1, 3, and 5% (w/w) concentrations for 2.5, 5.5, 10, 30 and 50 mg/kg dose level groups, respectively. The positive control, Na OH, was diluted to a final concentration of 5% (w/w) in Milli-Q water. Suitable aliquots of the test and positive control substances were weighed out and diluted to volume with vehicle. Test substance and control formulations were prepared weekly and stored in septum-capped containers at room temperature under a hood. All dosing formulation concentrations were confirmed during Weeks 1 and 2 and were within 3% of the theoretical concentration. The stability of the high and low concentration test substance dosing formulations was determined over 8 and 13-day periods. Both concentrations were still

stable after 13 days. The methodology used and the analytical results are detailed in Appendix B. The dose formulations used in the blood gas study were similarly prepared, except the 25% TMAH dose was not diluted in vehicle (*i.e.*, used neat).

C. Animals: Male and female Sprague-Dawley rats, approximately 5 weeks of age, were purchased from Charles River Laboratories, Portage, MI, for use in this study. The animals were received on May 12, 1999 and a random sample (approximately 15%) of the shipment weighed 76 - 139 g the next day. Additional rats, for blood gas determinations, were received on June 30, 1999 and a random sample (25%) of the shipment weighed 74 - 128 g the next day. The rats were held in quarantine for approximately two weeks during which time they were observed daily for survival. Rats were acclimated to plastic collars by having the collars placed around each animal's neck for approximately 2, 4 and 6 hours on three days during the quarantine period. At the end of the quarantine period the rats were examined carefully to ensure their health and suitability as test subjects. Animals were randomly assigned to experimental groups using a randomization program that blocks for body weight. Rats selected for the study were identified by a uniquely numbered metal tag inserted through the pinna of the right ear and by a cage card bearing the corresponding identification number.

D. Food and Water: Certified Purina Rodent Chow 5002 (PMI Feeds, Inc., St. Louis, MO) was provided *ad libitum*, except during a scheduled overnight fasting period prior to terminal sacrifice. City of Chicago municipal water was available *ad libitum* by means of an automatic watering system. No known contaminants were present in the food or water of the animals which would have interfered with the outcome of the study. Reports for the food and water analyses are maintained with facility records.

E. Housing and Environment: The rats were housed individually in suspended stainless steel cages. Absorbent cage liners were placed in the pan below the stainless steel mesh floor of each animal cage to absorb liquids. During the treatment phase of the study, the animal room temperature ranged from 22.0 to 25.5°C and the relative humidity ranged from 27.3 to 69.0%. Fluorescent lighting was provided for 12 hours followed by 12 hours of darkness.

F. Experimental Design: Rats used for test substance exposure were selected at random and assigned to seven groups of ten males and ten females. In addition, six or eight

rats/sex/group were later added for blood gas analyses. A summary of the groups is outlined below.

Dermal Toxicity Study:

Group		Test Material	Dose Level (w/w)	No. rats/group Male	Female
1	Vehicle Control	DI water	0 %	10	10
2	Low	TMAH	0.25 %	10	10
3	Mid-Low	TMAH	0.55 %	10	10
4	Mid	TMAH	1 %	10	10
5	Mid-High	TMAH	3 %	10	10
6	High	TMAH	5 %	10	10
7	Positive Control	NaOH	5 %	10	10

Blood Gas Analyses:

Group		Test Material	Dose Level (w/w)	No. rats/group Male	Female
8	Vehicle Control	DI water	0 %	6	6
9	High	TMAH	5 %	6	6
10	Neat (undiluted)	TMAH	25 %	6+2	6+2

Dosing for the four-week dermal toxicity was initiated on May 25, 1999 for the male rats and May 26, 1999 for the females. Due to the severe skin irritation noted for all rats in the positive control group, dosing was stopped on May 27, 1999 (Day 3 for males and Day 2 for females). The rats were removed from the study and subsequently euthanized and discarded without necropsy on June 7, 1999. No deaths or systemic toxicity was evident in this group of animals prior to their removal from the study. All surviving rats (*i.e.*, Groups 1-6) were necropsied on June 22 and 23, 1999.

On July 13, 1999, test or control formulation was applied to the skin of six rats per group for approximately 1 to 4 hours. Two rats/sex were added to the 25% TMAH group due to rats dying during blood collection for blood gas and hematology parameter measurements.

G. Methods

1. Skin Preparation: Approximately 24 hours prior to treatment, fur was clipped between the shoulders (*i.e.*, dorsal scapular region) and the skin examined for abnormalities. Rats found at that time to have significant skin abnormalities were excluded from the study. Toxicity study rats were shaved three times per week during the application period. The application site for the blood gas analysis rats was clipped on the day of dosing.

2. Dosing: For each group, dosing formulations were dispensed onto a Hill Top Chamber® (Hill Top Biolabs, Inc., Cincinnati, OH) at a constant dosing volume of 1 ml/kg of body weight, based upon the animals most recently determined weight. The chamber was then applied to the clipped shoulder blades of each rat and secured with an elastic band fastened with Velcro®. The toxicity study animals were exposed to the dosing formulations six hours /day, five days/week for four weeks beginning on May 25 (males) or May 26 (females), 1999. The blood gas study animals were exposed to the dosing formulations on July 13, 1999, for approximately 1-3 hours or until peak observation of clinical signs. Each animal was fitted with a plastic neck collar to prevent ingestion or grooming prior to dosing. Collars for toxicity study rats were fitted on Mondays prior to dosing and were removed on weekends (*i.e.*, Saturday mornings).

3. Clinical Observations: Study animals were observed twice daily on week days, once daily on weekends and holidays, for moribundity and mortality. Rats were observed for overt toxicity each time they were handled for treatment or survival checks. A detailed clinical observation including signs of dermal irritation was documented once each week at animal weighing and whenever a new observation was noted. The weekly observations were recorded by electronic data capture (LABCAT, IPA, Inc., Princeton, NJ, version 4.64).

4. Body Weights: Toxicity study animals were weighed at randomization, one day prior to initiating dosing and weekly thereafter. A fasted terminal body weight was also determined on the day of euthanasia. Body weights were recorded and gains calculated using electronic data capture (LABCAT). Blood gas study animals were weighed at randomization and on the day of treatment initiation (Day 1).

5. Food Consumption: Weekly food consumption was measured and coincided with weekly body weight determinations. Food consumption was recorded using electronic data capture (LABCAT).

6. Clinical Pathology Procedures and Urinalysis: Surviving toxicity study rats were transferred to metabolism cages on the day prior to scheduled sacrifice for overnight urine collection. Blood samples were collected on the day of sacrifice *via* the abdominal aorta under sodium pentobarbital anesthesia from surviving rats (fasted overnight, approximately 18 hours) for hematology and clinical chemistry evaluations. Hematological parameters evaluated using a Baker System 9000

analyzer (Biochem Immunosystems, Inc., Allentown, PA) consisted of total erythrocyte count, total leukocyte count, hematocrit, hemoglobin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration and platelet count. Hematological parameters evaluated microscopically consisted of erythrocyte morphology, differential leukocyte count (absolute), and reticulocyte count (absolute). Packed cell volume was also determined. The following clinical chemistry parameters were evaluated using a Beckman Synchron CX5 analyzer (Beckman Instruments, Inc., Brea, CA): glucose, urea nitrogen, creatinine, cholesterol, bilirubin, total bile acids, total protein, albumin, globulin, albumin/globulin ratio, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, creatine kinase, sorbitol dehydrogenase, triglycerides, phosphorus, sodium, calcium, potassium and chloride. Clinical pathology analyses were performed using LABCAT (IPA Inc., Princeton, NJ, version 4.41a). Clinical pathology methods are referenced in Appendix Q.

A microscopic evaluation of the urine collected was performed and the following parameters were observed or measured: urine volume, sodium and potassium levels, color, appearance, refractive index, specific gravity, and qualitative measurement of glucose, urobilinogen, pH, protein, ketone, blood, nitrites, leukocytes, creatinine and bilirubin. A key to interpretation of urinalysis data is presented in Appendix Q.

7. Evaluation of Acetylcholinesterase Activity: On study Days 2 and 24, blood samples for determination of acetylcholinesterase (AChE) activity were collected *via* the retroorbital sinus from anesthetized (70% CO_2/30% air) rats at least two hours after application of dosing formulations. A Beckman CX5 automated clinical chemistry analyzer was used in the assay and data were reported by computerized electronic data capture (LABCAT, IPA, Inc. Princeton, NJ, Version 4.41).

8. Blood Gas Evaluation: To investigate possible cause of death, 5% and 25% TMAH formulations were applied to the backs of six rats/sex/group as described in Sections II F and G.2. of this report. A third group used distilled water as a vehicle control. Approximately 1 to 4 hours following dose application, blood was collected from the abdominal aorta of sodium pentobarbitol anesthetized rats. Due to mortality during blood collection in the 25% TMAH group, two additional rats/sex were dosed. Blood from these animals was collected approximately

0.5 hour following exposure. Samples for blood gas analysis were held on ice and transported to the University of Illinois - Chicago for analysis. Blood gas analyses for pO_2, pCO_2, pH and HCO_3 were performed within 1-3 hours of collection. Blood also was collected from initially-dosed rats (6/sex/group) for analysis of hematology parameters, as described in Section II G.6.

9. Postmortem Examination Procedures: On the scheduled day of necropsy, fasted rats were exsanguinated under sodium pentobarbital anesthetic. Complete necropsies were performed on all toxicity-designated rats, except only gross necropsies were performed on the 5% TMAH rats or rats not surviving at least two days of TMAH exposure. Suspect lesions were collected from the gross necropsied rats. Necropsies were not performed on the positive control rats. The following tissues were collected from complete necropsy rats: adrenals, aorta, brain, [epididymides], esophagus, [eyes], [exorbital lacrimal gland], [femur], heart, cecum, colon, duodenum, ileum, jejunum, rectum, kidneys, liver, lung, lymph nodes (mesenteric and submandibular), ovaries, pancreas, pituitary, [prostate (with seminal vesicles)], salivary gland, sciatic nerve, [skeletal muscle], skin (untreated and from application site), [mammary gland], [spinal cord (cervical, lumbar and thoracic)], spleen, sternum (bone marrow), stomach, testes, thymus, thyroid (with parathyroids), trachea, urinary bladder, uterus, [zymbal gland] and gross lesions. All tissues were fixed in 10% neutral buffered formalin. Adrenals, brain, heart, kidneys, liver, ovaries, spleen and testes were weighed, and the organ to fasted body weight ratios were calculated.

   A complete set of tissues (excluding those in brackets) from all rats in the vehicle control group and in the two highest surviving dose groups (3% and 1%) were processed, stained with hematoxylin and eosin and examined microscopically by a board-certified veterinary pathologist. In addition, the skins (application site) in the Mid-low (0.55%) and Low (0.25%) groups were also sectioned and examined based on the findings from the Mid-high (3%) and High (5%) dose groups.

H. Statistical Procedures: Statistical analysis of continuous data was performed using analysis of variance followed, where appropriate, by Dunnett's test. All comparisons were performed using the vehicle control exposed animals as the control group. Analyses were performed by LABCAT or with SYSTAT software. A minimum significance level of $p \leq 0.05$ was used for all comparisons.

I. Deviations: Due to technical problems (*e.g.* inadvertent omission of data collection and missed arterial puncture) data for food consumption at week 3 for animal no. 356 and terminal blood collection for animal no. 378 are unavailable. Also, rats for the blood gas evaluations were not ear tagged due to the rapid turnabout of the study (*i.e.*, 1 to 4 hour exposure). Instead the individual animal numbers were identified on the rat's tail using a permanent marker. These deviations should not affect the integrity of the study.

J. Archives: Original data generated at IITRI during the study, specimens and a copy of the final report will be retained in the IITRI archives for five years, at which time the Sponsor will be consulted concerning final disposition of the archival materials.

III. RESULTS

A. Mortality (Table 2): All 5% TMAH-treated rats died during the study and mortality was observed in 8 of 10 (males and females) in the 3% TMAH-treated rats. Nine female and two male rats in the 5% dose group as well as two female rats in the 3% dose group died on Day 1. With the exception of one male and one female rat that died on Day 8, all the remaining male rats in the 5% dose group died on Days 2 - 3. As stated, deaths in the 3% group occurred as early as 1 day and up to 14 days after treatment initiation. Two rats/sex in the 3% group survived the entire duration of the study. No deaths were observed in the positive control, vehicle control, or in the 0.25, 0.55 and 1% (w/w) TMAH-treated groups.

B. Clinical Observations (Tables 3 and 4, Appendix C): Clinical signs of toxicity noted shortly after exposure included tremors, ptosis, hypoactivity, ataxia, dyspnea and convulsions in the 3% and/or 5% TMAH-treated groups. No overt signs of toxicity were observed in any rats in the 0.25, 0.55 and 1% TMAH-treated groups. Blanched application site skin was observed on day 1 in all 5% TMAH-treated male rats (except one); by day 2, five male rats in the 3% TMAH-treated also had blanched skin. Application skin for most 1% TMAH-exposed rats and some 0.55% TMAH-exposed appeared scabbed. The application site skin of all positive control animals was severely necrotic and eschar was noted prior to removal from the study on days 3 and 4. No overt sign of toxicity was noted for any positive control animal.

C. Body Weights (Tables 5 through 8, Appendices D and E): No significant differences in body weight were observed during the study. A significant decrease in mean body weight gain was observed during week 2 for the two surviving male rats in the 3% TMAH-treated group. No significant differences in body weight gains were observed

in any other test group, with the exception of a significant increase in weight gain for the positive control group at week 2 (males) and week 1 (females). This increase was most likely due to the treatment termination as well as termination of collar and wrapping on days 3 and 4.

D. Food Consumption (Tables 9 and 10, Appendix F): A significant decrease in food consumption was observed during week 2 for the two surviving male rats in the 3% TMAH-treated group; this corresponds to the decreased body weight gain noted above. No significant differences in food consumption were observed in any other test group.

E. Hematology (Tables 11 and 12, Appendices G and H): A significant decrease in mean corpuscular hemoglobin concentration was observed in the 1% female TMAH-treated rats. However, this decrease was not considered toxicologically significant since the decrease was very small and no other parameters were affected. Polychromasia, poikilocytosis and anisocytosis of minimal severity, 1+, were seen in the vehicle controls; a 1+ severity for these observations is commonly seen in rats and is considered a normal variation. The red blood cell morphological alterations for male and female rats in the test substance treated group appear to be similar to the vehicle control. No other significant differences were noted in the hematological parameters.

F. Clinical Chemistry (Tables 13 and 14, Appendix I): In the 3% TMAH dose level, the two surviving male rats exhibited a significant increase in cholesterol while the two surviving females exhibited a significant increase in total bile acids.

G. Urinalysis (Tables 15 and 16, Appendix J): Significant decreases in potasium levels were observed in the 0.25% male and in both males and females in the 3% TMAH-treated groups. In addition, significant decreases in urine creatinine values were observed in the 1% and 3% TMAH-treated female rats. The significant differences in the 3% male and female dose group were based on only two surviving animals. No other significant difference was noted in the urine parameters.

H. Acetylcholinesterase (AChE) Activity (Tables 17 and 18, Appendix K): AChE activity in plasma and red blood cells was not inhibited in TMAH-treated rats compared to the vehicle control on Days 2 or 24.

I. Blood Gas Analysis (Tables 19 through 21, Appendices L, M and N): A significant decrease in pH and an increase in PCO_2 was observed in both male and female rats treated with 25% TMAH. The 25% TMAH-treated males also had decreased HCO_3

levels, while male and female rats treated with 5% TMAH only had decreased PO_2 levels.

The two extra 25% TMAH-treated rats/sex bled (approximately 0.5 hour after treatment) prior to overt (tremors/convulsions) toxicity signs were not included in the statistical analyses. However, the same parameter trend (*i.e.* decrease in pH, PO_2 and HCO_3; and increase PCO_2) was observed in the female rats. The parameters for the male rats appeared similar to the vehicle control.

Corresponding hematology profiles for the blood gas group rats indicated an increase in hemoglobin in the 25% TMAH-treated males and an increase in mean corpuscular volume in the 25% TMAH-treated females as well as increases in mean corpuscular hemoglobin in the 5% and 25% TMAH-treated females. Alterations in erythrocyte morphology were noted in both sexes in each of the test substance treatment groups, but not in all animals and not in a consistently dose-related fashion. Polychromasia, poikilocytosis, anisocytosis, microcytosis, hypochromia and target cells of minimal severity, 1+ or 2+, were seen in the vehicle controls; these observations are commonly seen in rats and are considered normal variations.

J. Organ Weights (Tables 24 through 27, Appendices O and P): There were no significant differences in absolute or relative organ weights for any tissue weighed from male TMAH-treated rats. For female rats, a statistically significant increase in absolute organ weight was seen in the adrenals for the 3% TMAH-treated group. However, this difference is based on a group size of two rats and was not considered treatment-related.

K. Gross Pathology (Tables 22 and 23, Appendix R): Treatment-related gross necropsy findings included various dermal irritation observations at the application skin site (*i.e.*, thickened, pigmentation, scab/scaly) which increased in incidence with dose level. Red or dark red pigmented lungs were generally early deaths and thus correlated with congestion. Other findings were incidental, sporadic and not attributable to the test substance.

L. Histopathology (Appendix R): Necrosis at the application site was observed in 9 of 10 male rats (mean severity = 3.00) and 8 of 10 females (mean severity = 2.90) in the 3% dose group. Necrosis was also noted in one rat/sex in the 1% dose group (mean severity = 0.20), and in one female rat in the 0.55% dose group (mean severity = 0.20). Other microscopic skin findings were exudative scab, squamous epithelial hyperplasia and inflammation (acute, subacute, or chronic active) at all dose levels, including

controls. Although noted in the controls, the magnitude of these findings increased in incidence, severity and distribution with increasing dose concentration of TMAH. Pulmonary congestion was noted in the early deaths of the 3% TMAH-treated rats and was most likely the result of pulmonary compromise. In addition, thymic lymphoid necrosis was observed in the 3% group and may have been stress related.

Vacuolation was present in the livers of control and treated male and female rats. The incidence of vacuolation was elevated in the 3% TMAH males. The overall incidence of vacuolation was: 1 of 10, 0 of 10 and 7 of 9 males and 6 of 10, 6 of 10 and 3 of 8 females in the respective 0, 1, and 3% dose groups. Vacuolation was accompanied by membrane bound homogenous, eosinophilic intracytoplasmic material. Hepatocellular eosinophilic intracytoplasmic material was present in 7 of 9 male rats and 2 of 8 female rats in the 3% dose group. Individual hepatocyte necrosis was limited to only 3 of 9 male rats in the 3% dose group.

IV. DISCUSSION AND CONCLUSIONS

TMAH was administered dermally at concentrations of 0.25, 0.55, 1, 3 and 5% (w/w) to 10 Sprague-Dawley rats/sex/group. All of the rats in the 5% dose group and 8 of 10 (males and females) in the 3% dose group died. Nine of the females and two males in the 5% dose group died on Day 1. The majority of the male rats in the 5% dose group died on Days 2 and 3; however, one rat/sex survived until Day 8. Rats in the 3% dose group died intermittently between study days 1 and 14; however 2 rats/sex survived throughout the study. No deaths and no overt signs of toxicity were observed in 0.25, 0.55 and 1% dose group rats. Clinical signs of toxicity noted prior to death consisted of hypoactivity, ptosis, tremors, ataxia, dyspnea and convulsions.

Based on the blood gas profiles (25% and 5%), it appears that the rats died of an acid base disturbance, as indicated by the significant decrease in blood pH level (25% males and females), decreased HCO_3 (25% males) and increased PCO_2 (25% males and females) and decreased PO_2 (5% males and females).

No toxicologically significant effects were noted in the surviving groups' (1% or below) body weight, organ weights, food consumption, hematology, urinalysis and acetylcholinesterase activity. However, treatment-related histopathology was observed in liver vacoulation (males) with eosinophilic intracytoplasmic material (males and females) and pulmonary congestion as a result of compromise was noted in the 3% TMAH-treated group (30 mg/kg/day).

In addition, TMAH was an apparent direct irritant at the 3% dose group as evidenced by significant necrosis which intermittently extended full thickness through the epidermis and dermis to the level of underlying skeletal muscle. The no effect levels for the most significant application site observations of necrosis and squamous epithelial hyperplasia were 0.55% in males and 0.25% in females, while the no effect level for systemic toxicity is 1% for both sexes.

V. QUALITY ASSURANCE STATEMENT

Study Title: Four-week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats

Project Numer: 1052

Study Number: 3

Study Director: John Findlay, B.S.

The portions of the 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 U.S. EPA Good Laboratory Practice Standards (40 CFR 792). The report describes the methods and procedures used in the study and the reported results accurately reflect the raw data of the study.

The following are the inspection dates, and the dates inspection findings were submitted:

	Findings Reported to:	
Date of Inspection	Study Director	Management
April 26, 1999	April 26, 1999	April 29, 1999
May 26, 1999	May 26, 1999	May 28, 1999
May 26, 1999	May 26, 1999	June 2, 1999
June 1, 1999	June 1, 1999	June 1, 1999
June 9, 1999	June 9, 1999	June 9, 1999
June 17, 1999	June 17, 1999	June 17, 1999
June 18, 1999	June 18, 1999	June 18, 1999
June 22, 1999	June 22, 1999	June 22, 1999
June 22, 1999	June 22, 1999	June 24, 1999
June 29, 1999	June 29, 1999	June 30, 1999
July 13, 1999	July 13, 1999	July 20, 1999
August 2, 1999	August 2, 1999	August 2, 1999
October 11-15, 18-22, 1999	October 22, 1999	January 13, 2000
January 11-14, 2000	January 14, 2000	May 3, 2000
May 4, 2000	May 4, 2000	May 4, 2000

R. A. Boyne 5/8/00

Ronald A. Boyne, B.S. Date
Manager, Quality Assurance

VI. TABLES

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Table 1

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	- basophils (absolute: thousands of cells/cubic millimeter blood; relative: percent leukocytes counted)
BIL	- bilirubin (milligrams / deciliter urine)
BLD	- blood
BUN	- blood urea nitrogen (milligrams nitrogen / deciliter serum)
CA	- calcium (milligrams / deciliter serum)
CL	- chloride (milliequivalents / liter serum)
CHOL	- cholesterol (milligrams / deciliter serum)
CK	- creatine kinase (international units / liter serum)
CREA	- creatinine (milligrams / deciliter serum or urine)
ECHE	- erythrocyte acetylcholinesterase (units / liter)
EOSIN	- eosinophils (absolute: thousands of cells/cubic millimeter blood; relative: percent leukocytes counted)
F	- female
GLOB	- globulin (grams / deciliter serum)
GLU	- glucose (milligrams / deciliter serum)
HCT	- hematocrit (percent)
HGB	- hemoglobin (grams / deciliter blood)
K	- potassium (milliequivalents / liter serum or urine)
KET	- ketones (milligrams / deciliter urine)
Kg	- kilograms
LEU	- leucocytes
IMM (BAND) NEU	- immature neutrophils (absolute: thousands of cells / cubic millimeter blood; relative: percent leukocytes counted)
LYMPH	- lymphocytes (absolute: thousands of cells/cubic millimeter blood; relative: percent leukocytes counted)
M	- male
mg	- milligrams
MAT NEU	- mature neutrophils (absolute: thousands of cells / cubic millimeter blood; relative: percent leukocytes counted)
MCH	- mean corpuscular hemoglobin (picograms)
MCHC	- mean corpuscular hemoglobin concentration (percent)
MCV	- mean corpuscular volume (fl=femtoliter; 10^{-15} liter, mole to a cubicmicron)
MONO	- monocytes (absolute: thousands of cells/cubic millimeter blood; relative: percent leukocytes counted)
N	- number
NA	- sodium (milliequivalents /liter serum or urine)
Neg or 0	- negative (urinalysis)
NIT	- nitrite

Table 1 (cont.)

Abbreviations

Norm	- normal
NRBC	- nucleated red blood cells (number / 100 white blood cells)
PCHE	- plasma acetylcholinesterase (units / liter)
PCV	- packed cell volume (percent)
PLT	- platelet count (thousands / cubic millimeter blood)
PO4	- phosphate (milligrams / deciliter serum)
Poss.	- possible (clinical observations)
PRO	- protein (milligrams / deciliter urine)
RBC	- red blood cell count (millions of cells / cubic millimeter blood)
RETABS	- absolute reticulocyte count (thousands / cubic millimeter blood)
RETPC	- relative reticulocyte count (percent of total erythrocyte count)
RI	- refractive index
SD	- standard deviation
SDH	- sorbitol dehydrogenase (international units / liter serum)
SG	- specific gravity (g/ml)
TBA	- total bile acids (µmol / liter serum)
TBIL	- total bilirubin (milligrams / deciliter serum)
TG	- triglycerides (milligrams / deciliter serum)
TP	- total protein (grams protein / deciliter serum)
UBG	- urobilinogen (milligrams / deciliter urine)
WBC	- white blood cell count (thousands of cells / cubic millimeter blood); corrected for NRBC

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Table 2

Summary of Mortality Data
(10 rats/sex/group)

	Group	Test Material	Dose Level (w/w)	Mortality Incidence		
				Males	Females	Combined
1	Vehicle Control	DI water	0 %	0	0	0
2	Low	TMAH	0.25 %	0	0	0
3	Mid-Low	TMAH	0.55 %	0	0	0
4	Mid	TMAH	1 %	0	0	0
5	Mid-High	TMAH	3 %	8	8	16
6	High	TMAH	5 %	10	10	20
7	Positive Control[a]	NaOH	5 %	--	--	--

[a] Removed from study on Day 4, due to necrotic skin lesions

Table 3

SUMMARY OF OBSERVATION FREQUENCY

STUDY: 1052SN3 SEX: MALE

DOSE:(mg/kg)	0	2.5	5.5	10	30	50	50
GROUP:	1-M	2-M	3-M	4-M	5-M	6-M	7-M
Animal found dead	0	0	0	0	8	10	0
Terminal Sacrifice	0	0	0	0	0	0	10
Normal	10	10	10	10	10	10	10
Irritable	0	1	0	0	0	0	0
Redness around the eyes	0	1	1	0	1	0	0
Redness around nose fur	1	1	0	1	0	0	0
Lesion - scabbed	1	0	2	9	4	1	0
Poss. grooming irritation	2	0	3	2	3	0	0
Eschar	0	0	0	0	0	0	10
Total Number of Animals	10	10	10	10	10	10	10

Poss. = Possible

Incidence reflects the number of animals that exhibited the sign at some time during the study including one day prior to dosing.

Due to early deaths (Days 1 and 2) in the 30 and/or 50 mg/kg groups, clinical toxicity signs and application site (skin) observations were not captured electronically. Early clinical signs noted were hypoactivity, ptosis, ataxia, tremors, dyspnea and convulsions. The application skin appeared blanched. These findings were documented in the raw data.

Table 4

SUMMARY OF OBSERVATION FREQUENCY

STUDY: 1052SN3 SEX: FEMALE

DOSE:(mg/kg)	0	2.5	5.5	10	30	50	50
GROUP:	1-F	2-F	3-F	4-F	5-F	6-F	7-F
Animal found dead	0	0	0	0	8	10	0
Terminal Sacrifice	0	0	0	0	0	0	10
Normal	10	10	10	10	10	10	10
Lacrimation	0	0	1	0	0	0	0
Lesion - scabbed	0	0	3	10	5	1	0
Poss. grooming irritation	2	1	3	3	0	0	0
Eschar	0	0	0	0	0	0	10
Total Number of Animals	10	10	10	10	10	10	10

Poss. = Possible

Incidence reflects the number of animals that exhibited the sign at some time during the study including one day prior to dosing.

Due to early deaths (Days 1 and 2) in the 30 and/or 50 mg/kg groups, clinical toxicity signs and application site (skin) observations were not captured electronically. Early clinical signs noted were hypoactivity, ptosis, ataxia, and tremors. The application skin appeared blanched. A general study note documented these findings.

Table 5

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 1052SN3 SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	2.5 2-M	5.5 3-M	10 4-M	30 5-M	50 6-M	50 7-M
WEEK 0	MEAN	225	223	226	223	225	226	222
	S.D.	6.2	7.8	9.4	11.0	10.7	10.1	7.3
	N	10	10	10	10	10	10	10
WEEK 1	MEAN	265	260	264	260	271	256	259
	S.D.	9.6	6.7	10.7	14.1	9.6	--	8.4
	N	10	10	10	10	7	1	10
WEEK 2	MEAN	299	291	295	292	291	--	308
	S.D.	10.4	10.6	12.1	14.0	11.3	--	11.7
	N	10	10	10	10	2	0	10
WEEK 3	MEAN	336	325	333	327	333	--	--
	S.D.	12.7	14.6	14.0	17.5	16.3	--	--
	N	10	10	10	10	2	0	0
WEEK 4	MEAN	358	348	358	350	361	--	--
	S.D.	13.7	15.2	18.8	20.4	18.4	--	--
	N	10	10	10	10	2	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

Table 6

SUMMARY OF BODY WEIGHTS (Grams)

STUDY: 1052SN3 SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	2.5 2-F	5.5 3-F	10 4-F	30 5-F	50 6-F	50 7-F
WEEK 0	MEAN	162	161	161	162	162	161	162
	S.D.	8.1	8.9	8.6	9.1	8.3	8.2	8.6
	N	10	10	10	10	10	10	10
WEEK 1	MEAN	177	176	180	180	177	160	186
	S.D.	13.3	10.0	9.4	11.5	15.3	--	12.0
	N	10	10	10	10	5	1	10
WEEK 2	MEAN	201	198	201	205	202	--	--
	S.D.	18.5	9.7	12.9	15.4	16.4	--	--
	N	10	10	10	10	4	0	0
WEEK 3	MEAN	217	216	220	224	239	--	--
	S.D.	15.6	14.4	15.5	17.9	4.2	--	--
	N	10	10	10	10	2	0	0
WEEK 4	MEAN	231	229	230	235	250	--	--
	S.D.	16.0	14.4	15.0	17.3	1.4	--	--
	N	10	10	10	10	2	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

Table 7

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 1052SN3 SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	2.5 2-M	5.5 3-M	10 4-M	30 5-M	50 6-M	50 7-M
WEEK 1	MEAN	39	37	38	37	42	39	37
	S.D.	6.3	5.8	3.1	5.8	7.7	--	5.0
	N	10	10	10	10	7	1	10
WEEK 2	MEAN	34	31	31	32	21*	--	49**
	S.D.	6.1	6.3	4.6	3.3	4.2	--	8.7
	N	10	10	10	10	2	0	10
WEEK 3	MEAN	37	35	38	34	42	--	--
	S.D.	4.2	8.3	4.6	6.2	4.9	--	--
	N	10	10	10	10	2	0	0
WEEK 4	MEAN	22	22	25	23	29	--	--
	S.D.	4.7	2.2	7.8	5.4	2.1	--	--
	N	10	10	10	10	2	0	0
TOTAL GAIN	MEAN	132	125	132	127	132	--	--
	S.D.	13.6	17.1	14.2	13.8	9.2	--	--
	N	10	10	10	10	2	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

Table 8

SUMMARY OF WEIGHT GAINS (Grams)

STUDY: 1052SN3 SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	2.5 2-F	5.5 3-F	10 4-F	30 5-F	50 6-F	50 7-F
WEEK 1	MEAN	14	15	19	18	13	12	23*
	S.D.	7.2	5.3	4.2	7.8	5.7	--	9.1
	N	10	10	10	10	5	1	10
WEEK 2	MEAN	25	22	21	25	20	--	--
	S.D.	7.5	3.6	4.4	6.7	7.3	--	--
	N	10	10	10	10	4	0	0
WEEK 3	MEAN	16	18	19	19	24	--	--
	S.D.	7.7	5.5	6.5	9.5	2.1	--	--
	N	10	10	10	10	2	0	0
WEEK 4	MEAN	14	14	10	12	11	--	--
	S.D.	7.6	4.6	5.5	7.2	2.8	--	--
	N	10	10	10	10	2	0	0
TOTAL GAIN	MEAN	69	68	68	74	77	--	--
	S.D.	12.8	11.1	10.2	12.8	1.4	--	--
	N	10	10	10	10	2	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

Table 9

SUMMARY OF FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 SEX: MALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-M	2.5 2-M	5.5 3-M	10 4-M	30 5-M	50 6-M	50 7-M
WEEK 1	MEAN	184	183	177	180	176	185	177
	S.D.	18.4	10.6	8.9	14.6	9.4	--	13.3
	N	10	10	10	10	7	1	10
WEEK 2	MEAN	196	191	185	192	168*	--	202
	S.D.	14.0	11.0	10.4	14.1	4.2	--	14.6
	N	10	10	10	10	2	0	10
WEEK 3	MEAN	212	214	204	207	221	--	--
	S.D.	12.9	18.2	9.6	18.3	7.1	--	--
	N	10	9	10	10	2	0	0
WEEK 4	MEAN	223	225	225	227	236	--	--
	S.D.	17.0	18.8	11.5	18.7	4.2	--	--
	N	10	10	10	10	2	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

Table 10

SUMMARY OF FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 SEX: FEMALE

PERIOD	DOSE: (mg/kg) GROUP:	0 1-F	2.5 2-F	5.5 3-F	10 4-F	30 5-F	50 6-F	50 7-F
WEEK 1	MEAN	143	138	142	139	143	126	144
	S.D.	10.3	11.5	10.4	12.6	13.2	--	11.5
	N	10	10	10	10	5	1	10
WEEK 2	MEAN	165	155	155	156	160	--	--
	S.D.	16.2	9.4	14.9	14.0	16.5	--	--
	N	10	10	10	10	4	0	0
WEEK 3	MEAN	176	168	171	167	186	--	--
	S.D.	13.3	13.1	12.4	16.9	4.2	--	--
	N	10	10	10	10	2	0	0
WEEK 4	MEAN	178	173	169	169	192	--	--
	S.D.	12.2	12.4	14.3	12.0	3.5	--	--
	N	10	10	10	10	2	0	0

* P less than .05
** P less than .01
-- = Data Unavailable

Analysis of Variance using DUNNETT'S Procedure

Table 11

SUMMARY OF HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
Group: Vehicle : Distilled Water 0 (w/w%)									
MEAN	7.9	7.20	14.8	41.0	43	57.0	20.6	36.0	1045
SD	2.66	0.244	0.32	1.28	1.4	1.47	0.70	0.87	98.9
N	10	10	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)									
MEAN	8.5	6.97	14.7	40.2	43	57.7	21.0	36.4	1096
SD	2.15	0.273	0.49	1.23	1.2	0.88	0.76	0.80	126.6
N	10	10	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)									
MEAN	9.2	7.23	15.0	41.5	43	57.5	20.7	36.0	1137
SD	3.59	0.245	0.50	1.34	1.6	1.54	0.70	0.57	187.4
N	9	9	9	9	9	9	9	9	9
Group: Mid : 1 (w/w%)									
MEAN	11.2	7.13	15.0	41.5	44	58.2	21.1	36.3	1118
SD	2.47	0.270	0.61	1.71	1.4	1.06	0.61	0.67	107.9
N	10	10	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)									
MEAN	10.0	7.53	15.5	43.1	45	57.2	20.6	36.0	1072
SD	0.00	0.354	0.42	1.63	0.0	0.49	0.42	0.42	57.3
N	2	2	2	2	2	2	2	2	2
Group: High : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0

NA-Not Applicable

Table 11 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
Group: Vehicle : Distilled Water 0 (w/w%)									
MEAN	4.4	316.2	0.0	1.2	6.6	0.1	0.1	0.0	0.0
SD	0.88	57.09	0.00	0.43	2.26	0.11	0.07	0.00	0.00
N	10	10	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)									
MEAN	4.2	288.4	0.0	1.1	7.3	0.1	0.1	0.0	0.0
SD	1.26	83.47	0.00	0.34	1.89	0.10	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)									
MEAN	4.3	307.9	0.0	1.3	7.7	0.2	0.0	0.0	0.0
SD	1.08	71.61	0.00	0.54	3.13	0.16	0.05	0.00	0.00
N	9	9	9	9	9	9	9	9	9
Group: Mid : 1 (w/w%)									
MEAN	4.1	294.4	0.0	1.4	9.5	0.2	0.1	0.0	0.0
SD	0.99	70.99	0.00	0.46	2.03	0.14	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)									
MEAN	4.0	299.8	0.0	1.7	8.2	0.2	0.0	0.0	0.0
SD	1.34	115.12	0.00	0.07	0.07	0.14	0.00	0.00	0.00
N	2	2	2	2	2	2	2	2	2
Group: High : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0

NA-Not Applicable

Table 12

SUMMARY OF HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
Group: Vehicle : Distilled Water 0 (w/w%)									
MEAN	6.3	6.63	13.9	38.5	41	58.0	20.9	36.1	1157
SD	1.26	0.275	0.45	1.44	1.9	1.33	0.58	0.51	104.9
N	10	10	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)									
MEAN	6.2	6.83	14.1	39.1	41	57.3	20.7	36.1	1130
SD	1.77	0.394	0.52	1.49	1.7	1.97	0.78	0.39	80.1
N	10	10	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)									
MEAN	7.0	6.74	14.1	39.5	41	58.7	21.0	35.8	1172
SD	4.22	0.607	1.08	2.98	3.2	1.84	0.64	0.49	261.1
N	10	10	10	10	10	10	10	10	10
Group: Mid : 1 (w/w%)									
MEAN	6.6	6.90	14.3	40.2	42	58.3	20.7	35.5*	1109
SD	1.79	0.380	0.63	1.91	2.3	1.55	0.73	0.49	48.9
N	10	10	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)									
MEAN	6.1	6.99	14.7	40.4	43	57.8	21.0	36.3	1104
SD	0.92	0.092	0.07	0.14	0.7	0.92	0.35	0.07	33.2
N	2	2	2	2	2	2	2	2	2
Group: High : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0
NA-Not Applicable
*-Significant Difference from Control P < .05

Table 12 (cont.)

SUMMARY OF HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE — SEX: FEMALE

TEST(s): / UNITS:	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
Group: Vehicle : Distilled Water 0 (w/w%)									
MEAN	3.7	243.4	0.0	0.7	5.4	0.1	0.0	0.0	0.0
SD	0.75	46.54	0.00	0.42	1.08	0.09	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)									
MEAN	3.9	261.5	0.0	0.7	5.4	0.1	0.0	0.0	0.0
SD	0.80	42.90	0.00	0.20	1.59	0.07	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)									
MEAN	3.9	257.5	0.0	0.8	6.1	0.1	0.1	0.0	0.0
SD	1.30	63.61	0.00	0.46	3.77	0.07	0.08	0.00	0.00
N	10	10	10	10	10	10	10	10	10
Group: Mid : 1 (w/w%)									
MEAN	3.4	232.4	0.0	0.9	5.6	0.1	0.1	0.0	0.0
SD	0.56	32.97	0.00	0.33	1.49	0.09	0.07	0.00	0.00
N	10	10	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)									
MEAN	3.1	212.9	0.0	0.8	5.2	0.1	0.1	0.0	0.0
SD	0.35	21.92	0.00	0.14	0.64	0.07	0.07	0.00	0.00
N	2	2	2	2	2	2	2	2	2
Group: High : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)									
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0

NA-Not Applicable

Table 13

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3

SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
Group: Vehicle : Distilled Water 0 (w/w%)							
MEAN	144	4.3	106	9.7	8.1	23	17
SD	1.6	0.45	2.3	0.28	0.50	4.1	5.7
N	10	10	10	10	10	10	7
Group: Low : 0.25 (w/w%)							
MEAN	144	4.2	105	9.6	8.0	24	15
SD	1.2	0.29	1.0	0.27	0.44	2.6	4.7
N	10	10	10	10	10	10	8
Group: Mid-Low : 0.55 (w/w%)							
MEAN	144	4.3	105	9.6	8.0	24	15
SD	0.9	0.17	0.8	0.20	0.49	3.8	3.6
N	9	9	9	9	9	9	6
Group: Mid : 1 (w/w%)							
MEAN	144	4.3	106	9.7	7.9	25	16
SD	1.5	0.25	0.9	0.30	0.60	2.5	6.6
N	10	10	10	10	10	10	6
Group: Mid-High : 3 (w/w%)							
MEAN	144	4.3	106	10.0	8.4	35**	19
SD	1.4	0.00	0.7	0.00	0.28	8.5	2.8
N	2	2	2	2	2	2	2
Group: High : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

**-Significant Difference from Control P < .01 NA-Not Applicable

Table 13 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	ALP	ALT	AST	TBIL	SDH	TBA
UNITS:	IU/L	IU/L	IU/L	IU/L	mg/dL	IU/L	umol/L
Group: Vehicle : Distilled Water 0 (w/w%)							
MEAN	897	174	30	123	0.49	12.6	43.8
SD	462.2	52.8	4.2	36.7	0.068	4.24	36.14
N	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)							
MEAN	1232	174	31	136	0.48	11.8	40.4
SD	507.6	50.8	3.0	28.5	0.070	3.00	19.79
N	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)							
MEAN	1181	162	30	137	0.53	11.0	51.9
SD	220.8	35.9	2.6	19.3	0.120	2.00	53.83
N	9	9	9	9	9	9	9
Group: Mid : 1 (w/w%)							
MEAN	1060	164	30	135	0.53	13.6	56.8
SD	557.8	22.1	3.6	31.3	0.050	5.13	38.80
N	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)							
MEAN	372	181	25	85	0.48	9.0	24.2
SD	272.2	18.4	1.4	21.2	0.007	0.57	7.00
N	2	2	2	2	2	2	2
Group: High : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA-Not Applicable

Table 13 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	BUN	CREA	GLU	TP	ALB	GLOB	A/G
UNITS:	mg/dL	mg/dL	mg/dL	g/dL	g/dL	g/dL	-
Group: Vehicle : Distilled Water 0 (w/w%)							
MEAN	15	0.5	103	5.2	3.6	1.6	2.2
SD	1.9	0.07	20.0	0.24	0.18	0.13	0.21
N	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)							
MEAN	14	0.4	106	5.1	3.5	1.6	2.3
SD	1.4	0.10	13.2	0.15	0.15	0.16	0.31
N	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)							
MEAN	16	0.5	102	5.2	3.5	1.7	2.1
SD	2.6	0.05	17.0	0.10	0.18	0.17	0.28
N	9	9	9	9	9	9	9
Group: Mid : 1 (w/w%)							
MEAN	16	0.5	107	5.3	3.6	1.7	2.2
SD	2.1	0.08	14.5	0.22	0.16	0.14	0.19
N	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)							
MEAN	13	0.4	96	5.2	3.4	1.8	2.0
SD	1.4	0.00	9.2	0.07	0.00	0.07	0.07
N	2	2	2	2	2	2	2
Group: High : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA-Not Applicable

Table 14

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	NA	K	CL	CA	PO4	CHOL	TG
UNITS:	mmol/L	mmol/L	mmol/L	mg/dL	mg/dL	mg/dL	mg/dL
Group: Vehicle : Distilled Water 0 (w/w%)							
MEAN	143	3.9	106	9.6	7.0	31	15
SD	1.6	0.17	1.5	0.21	0.84	7.8	4.5
N	10	10	10	10	10	10	7
Group: Low : 0.25 (w/w%)							
MEAN	143	3.8	106	9.6	7.1	29	13
SD	1.1	0.25	1.9	0.18	0.99	6.3	3.2
N	10	10	10	10	10	10	9
Group: Mid-Low : 0.55 (w/w%)							
MEAN	142	4.1	107	9.6	7.2	26	13
SD	1.0	0.78	1.9	0.28	1.17	5.2	2.3
N	10	10	10	10	10	10	7
Group: Mid : 1 (w/w%)							
MEAN	143	3.9	107	9.7	7.1	29	13
SD	0.8	0.21	1.5	0.20	0.56	6.5	2.0
N	10	10	10	10	10	10	7
Group: Mid-High : 3 (w/w%)							
MEAN	145	3.8	106	9.6	7.1	30	17
SD	0.0	0.35	0.7	0.07	0.21	4.2	1.4
N	2	2	2	2	2	2	2
Group: High : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA-Not Applicable

Table 14 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	CK	ALP	ALT	AST	TBIL	SDH	TBA
UNITS:	IU/L	IU/L	IU/L	IU/L	mg/dL	IU/L	umol/L
Group: Vehicle : Distilled Water 0 (w/w%)							
MEAN	1063	124	32	141	0.49	12.5	24.5
SD	422.6	35.3	7.4	30.5	0.046	1.71	4.92
N	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)							
MEAN	1178	113	31	146	0.50	15.0	24.6
SD	356.4	25.1	6.1	15.0	0.103	6.97	5.67
N	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)							
MEAN	1211	105	28	146	0.48	11.4	26.4
SD	422.9	37.8	5.2	29.7	0.090	2.32	7.91
N	10	10	10	10	10	10	10
Group: Mid : 1 (w/w%)							
MEAN	862	133	31	127	0.51	13.8	31.8
SD	268.3	39.4	7.0	19.2	0.089	5.30	9.92
N	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)							
MEAN	962	136	37	150	0.46	12.5	51.9**
SD	868.3	56.6	2.1	46.0	0.071	4.17	28.99
N	2	2	2	2	2	2	2
Group: High : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

**-Significant Difference from Control P < .01 NA-Not Applicable

Table 14 (cont.)

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	BUN	CREA	GLU	TP	ALB	GLOB	A/G
UNITS:	mg/dL	mg/dL	mg/dL	g/dL	g/dL	g/dL	-
Group: Vehicle : Distilled Water 0 (w/w%)							
MEAN	21	0.5	97	5.5	3.9	1.6	2.5
SD	3.0	0.09	11.4	0.25	0.19	0.12	0.21
N	10	10	10	10	10	10	10
Group: Low : 0.25 (w/w%)							
MEAN	18	0.5	96	5.5	4.0	1.5	2.7
SD	2.4	0.08	8.0	0.27	0.26	0.12	0.26
N	10	10	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)							
MEAN	20	0.5	100	5.5	3.9	1.6	2.5
SD	2.3	0.07	9.9	0.29	0.22	0.14	0.21
N	10	10	10	10	10	10	10
Group: Mid : 1 (w/w%)							
MEAN	19	0.5	94	5.4	3.9	1.5	2.7
SD	2.6	0.06	9.1	0.17	0.15	0.10	0.26
N	10	10	10	10	10	10	10
Group: Mid-High : 3 (w/w%)							
MEAN	19	0.5	99	5.4	3.8	1.7	2.3
SD	0.7	0.00	2.1	0.42	0.35	0.07	0.14
N	2	2	2	2	2	2	2
Group: High : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0
Group: (+)Control : 5 (w/w%)							
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA-Not Applicable

Table 15

Summary of Urinalysis Data - Males

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	NA	K	CREA	NA/CREA	K/CREA
UNITS:	mmol/L	mmol/L	mg/dL	-	-
Group: Vehicle : Distilled Water 0 (w/w%)					
MEAN	52	133.8	74.1	0.7	1.84
SD	20.9	37.97	23.40	0.25	0.197
N	10	10	10	10	10
Group: Low : 0.25 (w/w%)					
MEAN	32	88.6*	48.3	0.7	1.88
SD	13.6	33.46	20.07	0.27	0.251
N	10	10	10	10	10
Group: Mid-Low : 0.55 (w/w%)					
MEAN	46	113.2	65.2	0.8	1.75
SD	16.4	51.49	29.40	0.22	0.134
N	10	10	10	10	10
Group: Mid : 1 (w/w%)					
MEAN	56	107.7	61.7	0.9	1.78
SD	27.0	33.95	21.55	0.46	0.233
N	10	10	10	10	10
Group: Mid-High : 3 (w/w%)					
MEAN	20	52.3*	37.3	0.5	1.39
SD	0.7	17.61	3.68	0.00	0.332
N	2	2	2	2	2
Group: High : 5 (w/w%)					
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0
Group: (+)Control : 5 (w/w%)					
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0

*-Significant Difference from Control P < .05 NA-Not Applicable

Table 16

Summary of Urinalysis Data - Females

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE — SEX: FEMALE

TEST(s): / UNITS:	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
Group: Vehicle : Distilled Water 0 (w/w%)					
MEAN	32	96.1	55.6	0.6	1.73
SD	13.4	31.34	17.27	0.21	0.258
N	10	10	10	10	10
Group: Low : 0.25 (w/w%)					
MEAN	37	87.6	45.5	0.8	1.91
SD	20.0	38.41	17.90	0.34	0.167
N	9	10	10	9	10
Group: Mid-Low : 0.55 (w/w%)					
MEAN	42	113.6	65.4	0.6	1.76
SD	17.9	31.34	15.34	0.15	0.366
N	10	10	10	10	10
Group: Mid : 1 (w/w%)					
MEAN	24	65.8	37.8*	0.6	1.75
SD	15.3	19.45	9.01	0.36	0.359
N	10	10	10	10	10
Group: Mid-High : 3 (w/w%)					
MEAN	8	35.6*	18.5*	0.4	1.88
SD	0.7	15.41	4.31	0.14	0.396
N	2	2	2	2	2
Group: High : 5 (w/w%)					
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0
Group: (+)Control : 5 (w/w%)					
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0

*-Significant Difference from Control P < .05 NA-Not Applicable

Table 17

Summary of Acetylcholinesterase Activity Data - Males

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PCHE(C)	ECHE
UNITS:	U/L	U/L
Group: Vehicle : Distilled Water 0 (w/w%)		
MEAN	426	3936
SD	72.5	350.2
N	10	10
Group: Low : 0.25 (w/w%)		
MEAN	456	3910
SD	39.6	319.8
N	10	10
Group: Mid-Low : 0.55 (w/w%)		
MEAN	451	3913
SD	48.7	478.4
N	10	10
Group: Mid : 1 (w/w%)		
MEAN	439	3827
SD	54.1	344.9
N	10	10
Group: Mid-High : 3 (w/w%)		
MEAN	452	4004
SD	91.8	316.4
N	10	10
Group: High : 5 (w/w%)		
MEAN	420	3887
SD	52.1	259.1
N	7	7
Group: (+)Control : 5 (w/w%)		
MEAN	439	3970
SD	57.8	270.3
N	10	10

Table 17 (cont.)

Summary of Acetylcholinesterase Activity Data - Males

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PCHE(C)	ECHE
UNITS:	U/L	U/L
Group: Vehicle : Distilled Water 0 (w/w%)		
MEAN	434	3635
SD	72.7	423.4
N	10	10
Group: Low : 0.25 (w/w%)		
MEAN	480	3759
SD	53.8	323.8
N	10	10
Group: Mid-Low : 0.55 (w/w%)		
MEAN	469	3645
SD	55.0	381.3
N	10	10
Group: Mid : 1 (w/w%)		
MEAN	468	3556
SD	68.7	330.0
N	10	10
Group: Mid-High : 3 (w/w%)		
MEAN	486	3781
SD	94.0	123.0
N	2	2
Group: High : 5 (w/w%)		
MEAN	NA	NA
SD	NA	NA
N	0	0
Group: (+)Control : 5 (w/w%)		
MEAN	NA	NA
SD	NA	NA
N	0	0

NA-Not Applicable

Table 18

Summary of Acetylcholinesterase Activity Data - Females

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PCHE(C)	ECHE
UNITS:	U/L	U/L
Group: Vehicle : Distilled Water 0 (w/w%)		
MEAN	671	3906
SD	118.7	380.0
N	10	10
Group: Low : 0.25 (w/w%)		
MEAN	852	3826
SD	319.4	408.5
N	10	10
Group: Mid-Low : 0.55 (w/w%)		
MEAN	699	3971
SD	101.0	267.5
N	10	10
Group: Mid : 1 (w/w%)		
MEAN	610	4111
SD	97.6	279.3
N	9	9
Group: Mid-High : 3 (w/w%)		
MEAN	817	4085
SD	201.1	392.6
N	8	8
Group: High : 5 (w/w%)		
MEAN	933	3858
SD	NA	NA
N	1	1
Group: (+)Control : 5 (w/w%)		
MEAN	616	4021
SD	74.0	402.9
N	10	10

NA-Not Applicable

Table 18 (cont.)

Summary of Acetylcholinesterase Activity Data - Females

SUMMARY OF CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s):	PCHE(C)	ECHE
UNITS:	U/L	U/L
Group: Vehicle : Distilled Water 0 (w/w%)		
MEAN	1105	3720
SD	257.8	321.7
N	10	10
Group: Low : 0.25 (w/w%)		
MEAN	1285	3744
SD	549.0	469.6
N	10	10
Group: Mid-Low : 0.55 (w/w%)		
MEAN	1016	3532
SD	227.9	429.1
N	10	10
Group: Mid : 1 (w/w%)		
MEAN	932	3719
SD	230.6	416.7
N	10	10
Group: Mid-High : 3 (w/w%)		
MEAN	906	3698
SD	149.9	270.1
N	2	2
Group: High : 5 (w/w%)		
MEAN	NA	NA
SD	NA	NA
N	0	0
Group: (+)Control : 5 (w/w%)		
MEAN	NA	NA
SD	NA	NA
N	0	0

NA-Not Applicable

Table 19

Summary of Blood Gas Data

Dose Group	Dose Level (% w/w)	Sex		Parameter pH	PCO_2	PO_2	HCO_3
8 - Vehicle Control	0	M	Mean	7.249	59.6	201	26.4
			SD	0.0150	3.17	31.5	1.26
			N	6	6	6	6
9 - TMAH	5	M	Mean	7.259	58.4	144*	26.3
			SD	0.0228	4.59	18.4	0.76
			N	6	6	6	6
10 - TMAH	25	M	Mean	7.010*	94.5*	214	24.0*
			SD	0.0327	11.74	49.2	1.67
			N	5	5	5	5
TMAH[a]	25	M	Mean	7.266	56.8	165	26.1
			SD	0.0078	2.12	18.4	1.41
			N	2	2	2	2
8 - Vehicle Control	0	F	Mean	7.252	57.8	224	25.7
			SD	0.0437	4.05	51.2	1.29
			N	6	6	6	6
9 - TMAH	5	F	Mean	7.243	58.2	159*	25.3
			SD	0.0303	6.07	13.2	1.27
			N	6	6	6	6
10 - TMAH	25	F	Mean	6.957*	103.1*	198	23.3
			SD	0.0341	7.06	45.7	1.47
			N	5	5	5	5
TMAH[a]	25	F	Mean	6.990	93.2	88	22.7
			SD	0.0778	7.57	7.1	2.19
			N	2	2	2	2

[a] Extra rats; data not included in statistical analyses (blood collected approximately 0.5 hour after dosing)

* Significantly different from Vehicle Control (same sex), $p \leq 0.05$

Table 20

Summary of Hematology Data - Males (Blood Gas Animals)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
Group: Control : DI Water									
MEAN	5.8	5.45	12.4	34.6	37	63.5	22.8	35.9	1068
SD	1.65	0.200	0.36	1.04	1.1	1.82	0.79	0.47	117.1
N	6	6	6	6	6	6	6	6	6
Group: 5% : TMAH									
MEAN	5.3	5.60	12.5	34.7	37	61.9	22.3	36.0	1128
SD	1.19	0.264	0.29	1.46	1.5	0.74	0.63	0.77	122.9
N	6	6	6	6	6	6	6	6	6
Group: 25% : TMAH									
MEAN	6.1	5.67	12.9*	35.9	37	63.3	22.8	36.0	985
SD	3.15	0.186	0.31	0.61	1.1	1.57	0.67	0.59	44.5
N	5	5	5	5	5	5	5	5	5

WBC corrected for NRBC > 0

*-Significant Difference from Control P < .05

Table 20 (cont.)

Summary of Hematology Data - Males (Blood Gas Animals)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: MALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
Group: Control : DI Water									
MEAN	9.9	538.5	0.0	0.6	5.1	0.1	0.1	0.0	0.0
SD	2.25	118.52	0.00	0.18	1.57	0.10	0.05	0.00	0.00
N	6	6	6	6	6	6	6	6	6
Group: 5% : TMAH									
MEAN	8.5	477.4	0.0	0.6	4.7	0.1	0.0	0.0	0.0
SD	1.87	107.82	0.00	0.19	1.08	0.05	0.00	0.00	0.00
N	6	6	6	6	6	6	6	6	6
Group: 25% : TMAH									
MEAN	11.2	634.8	0.4	0.8	5.1	0.1	0.0	0.0	0.0
SD	2.99	165.08	0.89	0.43	2.72	0.11	0.04	0.00	0.00
N	5	5	5	5	5	5	5	5	5

WBC corrected for NRBC > 0

Table 21

Summary of Hematology Data - Females (Blood Gas Animals)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
Group: Control : DI Water									
MEAN	4.7	5.22	11.6	32.3	35	61.8	22.3	36.1	1165
SD	1.08	0.177	0.39	1.46	1.5	1.53	0.67	0.71	203.9
N	6	6	6	6	6	6	6	6	6
Group: 5% : TMAH									
MEAN	4.3	5.26	12.2	33.3	36	63.3	23.2*	36.7	1218
SD	0.79	0.151	0.37	1.03	1.2	0.79	0.21	0.66	45.7
N	6	6	6	6	6	6	6	6	6
Group: 25% : TMAH									
MEAN	5.7	5.18	12.1	33.2	35	64.1*	23.3*	36.3	1078
SD	3.63	0.443	0.60	2.42	2.2	1.68	0.88	1.01	17.7
N	4	4	4	4	4	4	4	4	4

WBC corrected for NRBC > 0

*-Significant Difference from Control P < .05

Table 21 (cont.)

Summary of Hematology Data - Females (Blood Gas Animals)

SUMMARY OF HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: FEMALE

ANALYSIS OF VARIANCE FOLLOWED BY DUNNETT'S PROCEDURE

TEST(s): / UNITS:	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
Group: Control : DI Water									
MEAN	9.9	517.6	0.3	0.6	4.0	0.1	0.0	0.0	0.0
SD	2.21	120.53	0.82	0.33	0.76	0.08	0.05	0.00	0.00
N	6	6	6	6	6	6	6	6	6
Group: 5% : TMAH									
MEAN	7.5	395.0	0.0	0.5	3.8	0.0	0.0	0.0	0.0
SD	1.25	67.08	0.00	0.08	0.69	0.05	0.04	0.00	0.00
N	6	6	6	6	6	6	6	6	6
Group: 25% : TMAH									
MEAN	9.8	507.1	0.5	0.5	5.2	0.0	0.0	0.0	0.0
SD	2.06	133.65	1.00	0.29	3.37	0.00	0.00	0.00	0.00
N	4	4	4	4	4	4	4	4	4

WBC corrected for NRBC > 0

Table 22

Summary of Gross Necropsy Observations - Males[a]

Organ and/or Observation	Vehicle Control	Dose Level (% w/w) 0.25	0.55	1	3	5
Skin (application site)						
- crust/lesion	2	--[b]	1	3	3	1
- pigmentation (dark, pale, blanched)	--	--	--	--	4	10
- lesion (scaly)	--	--	--	--	2	--
- thickened/thick	--	--	--	--	--	6
Lesion						
- face-crust (around eyes)	--	--	1	--	--	--
Lung						
- parenchyma-pigmentation (dark, red)	--	--	--	--	7	4
Cavities						
- cranial-fluid (red)	--	--	--	--	1	--
Lymph node						
- mandibular-enlarged	1	--	--	--	--	--
Thymus						
- pigmentation	1	--	--	--	--	--
Urinary bladder						
- lumen-calculus	--	--	--	--	1	--
Total Number of Animals	10	10	10	10	10	10

[a] Total number of rats having the observation.
[b] -- = Zero incidence

Table 23

Summary of Gross Necropsy Observations - Females[a]

Organ and/or Observation	Vehicle Control	Dose Level (% w/w) 0.25	0.55	1	3	5
Skin (application site)						
-crust/lesion	1	2	2	7	4	--[b]
-pigmentation (dark, brown, red)	--	--	--	--	4	9
-lesion (scaly)	--	--	--	--	2	1
-thick	--	--	--	--	2	--
Lung						
- parenchyma-pigmentation (dark, red, dark red)	--	--	--	--	1	8
Ovary						
- pigmentation (red)	--	--	--	--	1	5
- enlarged	1	--	--	--	--	--
- cyst	--	--	1	--	--	--
Uterus						
- dilatation	--	--	1	--	--	--
Liver						
- mass	--	--	1	--	--	--
Thymus						
- pigmentation (red)	1	1	--	--	--	--
Total Number of Animals	10	10	10	10	10	10

[a] Total number of rats having the observation.
[b] -- = Zero incidence

Table 24

Summary of Absolute Organ Weight Data - Males

Dose Group (% w/w)		Body Weight (g)	Absolute Organ Weight (g)						
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes
1 - Vehicle Control (0)	Mean	323	0.073	2.02	1.33	2.66	9.68	0.69	3.23
	SD	16.9	0.011	0.061	0.129	0.188	1.439	0.147	0.336
	N	10	10	10	10	10	10	10	10
2 - TMAH (0.25)	Mean	316	0.073	2.04	1.28	2.66	8.97	0.68	3.36
	SD	15.8	0.009	0.103	0.099	0.240	0.711	0.051	0.242
	N	10	10	10	10	10	10	10	10
3 - TMAH (0.55)	Mean	327	0.070	2.00	1.25	2.71	9.61	0.67	3.24
	SD	18.5	0.012	0.066	0.132	0.141	0.958	0.094	0.204
	N	10	10	10	10	10	10	10	10
4 - TMAH (1)	Mean	314	0.073	2.02	1.23	2.64	8.99	0.64	3.34
	SD	18.5	0.013	0.060	0.103	0.202	0.639	0.087	0.264
	N	10	10	10	10	10	10	10	10
5 - TMAH (3)	Mean	328	0.056	2.05	1.32	2.82	9.52	0.69	3.28
	SD	12.0	0.019	0.120	0.163	0.177	0.417	0.042	0.113
	N	2	2	2	2	2	2	2	2

Table 25

Summary of Absolute Organ Weight Data - Females

Dose Group (% w/w)		Body Weight (g)	Absolute Organ Weight (g)						
			Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen
1 - Vehicle Control (0)	Mean	213	0.068	1.96	0.86	1.86	7.03	0.106	0.52
	SD	14.4	0.007	0.046	0.080	0.158	0.908	0.026	0.081
	N	10	10	10	10	10	10	10	10
2 - TMAH (0.25)	Mean	209	0.070	1.88	0.90	1.85	6.87	0.105	0.52
	SD	14.2	0.013	0.113	0.063	0.135	0.789	0.017	0.046
	N	10	10	10	10	10	10	10	10
3 - TMAH (0.55)	Mean	210	0.067	1.91	0.91	1.85	6.82	0.100	0.57
	SD	13.8	0.011	0.050	0.044	0.117	0.902	0.029	0.106
	N	10	10	10	10	10	10	10	10
4 - TMAH (1)	Mean	215	0.075	1.92	0.89	1.90	6.77	0.116	0.51
	SD	15.9	0.007	0.127	0.097	0.204	0.728	0.021	0.066
	N	10	10	10	10	10	10	10	10
5 - TMAH (3)	Mean	234	0.091*	1.87	1.04	1.89	7.24	0.127	0.50
	SD	0.7	0.000	0.035	0.064	0.205	0.014	0.037	0.049
	N	2	2	2	2	2	2	2	2

* Significantly different from the vehicle control; $p \leq 0.05$

Table 26

Summary of Relative Organ-to-Body Weight[a] Data - Males

Dose Group (% w/w)		Relative Organ-to-Body Weight (%)						
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes
1 - Vehicle Control (0)	Mean	0.023	0.626	0.411	0.825	2.995	0.212	1.005
	SD	0.004	0.034	0.035	0.051	0.391	0.039	0.137
	N	10	10	10	10	10	10	10
2 - TMAH (0.25)	Mean	0.023	0.647	0.405	0.842	2.840	0.216	1.067
	SD	0.003	0.043	0.036	0.059	0.167	0.013	0.098
	N	10	10	10	10	10	10	10
3 - TMAH (0.55)	Mean	0.021	0.614	0.383	0.831	2.939	0.204	0.992
	SD	0.004	0.043	0.036	0.057	0.244	0.023	0.068
	N	10	10	10	10	10	10	10
4 - TMAH (1)	Mean	0.023	0.645	0.391	0.841	2.860	0.205	1.063
	SD	0.005	0.046	0.024	0.058	0.166	0.025	0.077
	N	10	10	10	10	10	10	10
5 - TMAH (3)	Mean	0.017	0.624	0.401	0.859	2.910	0.211	1.003
	SD	0.005	0.014	0.035	0.022	0.234	0.005	0.071
	N	2	2	2	2	2	2	2

[a] Relative Organ-to-Body Weight = [Organ Weight (g) ÷ Body Weight (g)] x 100

Table 27

Summary of Relative Organ-to-Body Weight[a] Data - Females

Dose Group (% w/w)		Relative Organ-to-Body Weight (%)						
		Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen
1 - Vehicle Control (0)	Mean	0.032	0.928	0.407	0.875	3.308	0.050	0.245
	SD	0.005	0.062	0.032	0.055	0.381	0.010	0.027
	N	10	10	10	10	10	10	10
2 - TMAH (0.25)	Mean	0.034	0.903	0.433	0.886	3.284	0.050	0.251
	SD	0.007	0.063	0.036	0.052	0.322	0.009	0.021
	N	10	10	10	10	10	10	10
3 - TMAH (0.55)	Mean	0.032	0.913	0.437	0.881	3.256	0.048	0.271
	SD	0.005	0.076	0.036	0.057	0.413	0.013	0.051
	N	10	10	10	10	10	10	10
4 - TMAH (1)	Mean	0.035	0.894	0.412	0.886	3.157	0.054	0.236
	SD	0.004	0.054	0.024	0.074	0.280	0.011	0.024
	N	10	10	10	10	10	10	10
5 - TMAH (3)	Mean	0.039	0.799	0.443	0.807	3.101	0.054	0.212
	SD	0.000	0.018	0.029	0.090	0.015	0.016	0.021
	N	2	2	2	2	2	2	2

[a] Relative Organ-to-Body Weight = [Organ Weight (g) ÷ Body Weight (g)] x 100

VII. APPENDICES

Appendix A: Protocol and Protocol Amendments

PROTOCOL

1. Title: Four-Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats

2. Sponsor: IBM Corporation
P.O. Box 1900
Boulder, CO 80301-9191

3. Testing Facility: IIT Research Institute
10 West 35th Street
Chicago, IL 60616

4. Objective: The objective of the study is to determine the toxicity of the test substance when applied repeatedly to the intact skin of rats.

5. Duration: The duration of the study will be 4 weeks.

6. Proposed Study Dates:

   a. Treatment Initiation: May 25, 1999
   b. Biophase Termination: June 23, 1999
   c. Draft Report Completion: September 23, 1999

7. Protocol Approval:

   a. Study Director: John Findlay Date: 5/21/99
   John Findlay, B.S.

   b. Manager of Research: Bernadette Ryan Date: 5/24/99
   Bernadette Ryan, Ph.D., D.A.B.T.

   c. Sponsor Representative: B. Brooks Date: 5/24/99
   Bradford Brooks, Ph.D.

8. This protocol complies with specific requirements of the Sponsor.

9. Test Substance:

   a. Identification: The test substance has been identified by the Sponsor as Tetramethylammonium Hydroxide, 25% [(TMAH). Its physical description and batch and/or lot number(s) will be documented in the raw data book. The vehicle for the test substance is DI water.

   b. Assay: Characterization of the bulk test substance is the responsibility of the Sponsor. Analysis of the test substance dosing formulations will be performed by IITRI at least twice during the study. Stability of the dosing formulations will be determined in at least the high and low concentrations by IITRI.

   c. Preparation and Storage: The bulk test substance and vehicle will be stored at room temperature (approximately 22°C) protected from light. The test substance formulations will be prepared weekly and stored in septum capped (vapor control) container at room temperature under a hood.

   d. Handling Precautions: When working with the test substance, personnel should wear eye **protection, dust/mist respirator, tyvek sleeves, apron, and two pairs of gloves (latex over polyethylene).**

   e. Test Substance Disposition: Reserve samples will be retained by the Sponsor. At the time of study termination, arrangements will be made for the return of any residual test substance and vehicle to the Sponsor. IITRI will not be required to retain any samples.

   f. Route of Administration: Dermal application.

10. Test System:

   a. Model: Seventy-five male and 75 female Sprague-Dawley rats (Charles River Laboratories, Portage, MI) will be used in this study. Rats will be approximately 4-5 weeks old and weigh approximately 75 to 100 grams upon arrival from the supplier, and will be approximately 6-8 weeks of age at the time of treatment initiation.

   b. Justification for Selection: The Sprague-Dawley rat is a model widely used for toxicity testing. A significant body of experience with this animal exists against which its reaction to the test substance can be evaluated, and it meets the requirements of relevant test standards.

   c. Housing: Rats will be single-housed in suspended stainless steel wire cages (approximately 25 x 18 x 18 cm) during the study.

   d. Cleaning and Sanitation: Animal rooms and cages will be cleaned and sanitized prior to housing animals in them. Cages and racks will be cleaned, sanitized and changed every two weeks. The changing of cages and racks will be documented in the study notebook. Absorbent animal cage boards will be placed in the dropping trays under the suspended cages and will be replaced at intervals of no more than four days.

e. Food: Certified Purina Rodent Chow #5002 (PMI Feeds Inc., St. Louis MO) will be provided **ad libitum** except during scheduled fasting periods. Manufacturer's analytical results from the lot(s) of diet used in the study will be maintained in a central file at IITRI. To the best of our knowledge no known contaminants are expected to be present in the diet that would interfere with the test substance or test system and would confound the interpretation of the study.

f. Water: City of Chicago water will be provided **ad libitum** by means of an automatic animal watering system. The water is periodically monitored for bacterial contamination and chemical composition (electrolytes, metals, etc.); the results of this monitoring are maintained in a central file at IITRI. There are no known levels of contaminants in the drinking water that will adversely impact the integrity of the study.

g. Animal Identification: Temporary identification numbers will be assigned to the animals prior to randomization. A permanent number will be assigned to each animal following randomization. A permanent number tag will be inserted through the pinna of the right ear. Each animal will have a permanent numerical identifier which is unique within the study. The animal and study numbers will be displayed on individual cage cards.

h. Environmental Control: Animal rooms will be lighted with fluorescent lights and maintained on a 12-hour light/12-hour dark cycle. Room temperature and humidity readings will be recorded daily and regulated to avoid extreme fluctuations.

11. Experimental Design:

The study will be composed of 7 groups consisting of 10 rats/sex/group. Five groups will be dosed with graded concentrations of the test substance formulation, whereas the sixth group will serve as a vehicle control and will be dosed with DI water. A seventh group will be treated with 5% sodium hydroxide and serve as a positive control. The test substance formulations will be administered dermally, at a constant volume of 1 ml/kg, for 6 hours/day, five days/week for 4 weeks. Prior to administration of the first dose and weekly thereafter, the dorsal skin of the rats will be clipped clean of fur. The test substance formulation will be applied to the reservoir of a Hill Top Chamber® (Hill Top Biolabs, Inc., Cincinnati, Ohio) which will be placed behind the animal's shoulder blades and secured with an elastic band fastened with Velcro®. In order to prevent any potential ingestion of the test substance formulation, each animal will be fitted with a plastic neck collar. The neck collar will remain on the animals neck on weekdays only (i.e., five days/week) throughout the 4 week dosing period. In addition, acetylcholinesterase (AChE) inhibition will be measured at two intervals on Day 2 and at the end of the study. The study design is outlined below:

Group	Dose Level (w/w%)	No. rats/group (♂)	(♀)
Vehicle Control (Distilled water)	0	10	10
Low dose	0.25	10	10
Mid-Low dose	0.55	10	10
Mid dose	1	10	10
Mid-High dose	3	10	10
High dose	5	10	10
Positive Control (5% sodium hydroxide)	5	10	10

12. Method:

a. Quarantine: The rats purchased for use in this study will be held in quarantine for at least 10 days prior to treatment initiation. Rats will be acclimated to the plastic collars by placing the collars around each animal's neck for a period of 2-6 hours on at least 3 days during the quarantine period.

b. Selection of Subjects: Each rat will be shaved, weighed and will receive a thorough physical examination to ensure its suitability for use as a test animal. Suitability will be based upon the animal's health status and body weight. The rats used on-test will be selected randomly from a pool of suitable animals.

c. Skin Preparation: Rats will be clipped clean of fur between the shoulders (*i.e.*, dorsal scapular region) prior to randomization. Fur will be clipped prior to test substance administration and at least weekly thereafter, if necessary and feasible. Any mechanical trauma to the skin resulting from shaving will be noted in the study record.

d. Test substance Application: Graded concentrations of the test substance, or vehicle, will be applied via the Hill Top Chamber® to the skin on the back of each rat 6 hours/day, five days/week, for 4 weeks. A dosing volume of 1 ml/kg will be used. Dosages will be adjusted to the most current body weight. The Hill Top Chamber® will be held in place with an elastic band secured with Velcro®. The chamber will be removed 6 hours after dosing. A collar will be placed around the neck of the animal to prevent grooming and will be removed on weekends (i.e., Saturday morning and replaced on Monday prior to dosing).

e. Injured or Diseased Animals: Animals on test will not be treated for any disease or injury. A complete record of the circumstances and disposition of affected animals will be made in the study notebook.

13. Observations:

a. Moribundity and Mortality: All rats will be observed at least once each day prior to the initiation of treatment. During the treatment period, rats will be observed twice daily on weekdays, and once daily on weekends and holidays. Any rat judged as moribund (i.e., clinical signs consisting of but not limited to the following: ataxia, loss or reduced righting reflex, hypothermia, reduced response to external stimuli) and not likely to survive until the next scheduled observation period will be removed, sacrificed and necropsied. These animals will be recorded as sacrificed *in extremis* in the study notebook. Dead animals will be removed immediately for necropsy and the death will be documented in the study notebook.

b. Toxicity: Rats will be observed for signs of overt toxicity each time they are handled for treatment or survival checks. A detailed clinical observation including documentation of any adverse skin reaction will be performed once each week at the time of weighing. In addition, any overt clinical signs of toxicity, including changes in the skin that were not observed at the weekly observation will be documented when present.

c. Physical Examination: A complete physical examination will be performed prior to treatment initiation and the results used for test animal selection. Another physical examination will be performed at the termination of the study.

d. Body Weight: Each rat will be weighed during quarantine for randomization purposes, one day prior to treatment initiation (day 0) of the study and weekly thereafter for the duration of the study. A fasted terminal body weight will be collected for all rats.

e. Food Consumption: Food consumption will coincide with body weights during the study and will be monitored weekly.

14. Clinical Pathology: Blood samples will be obtained from all rats via the abdominal aorta at the end of the study (after 4 weeks of treatment). On the day before scheduled sacrifice the rats will be transferred to metabolism cages for overnight urine collection, and will be fasted during this time for approximately 18 hours prior to blood collection. Immediately prior to blood collection the rats will be anesthetized with sodium pentobarbital. The following parameters will be measured:

a. Hematology

Hematocrit
Hemoglobin
Total Erythrocyte Count (RBC)
Total Leukocyte Count (WBC)
Differential Leukocyte Count (Absolute)
Mean Corpuscular Volume
Mean Corpuscular Hemoglobin
Mean Corpuscular Hemoglobin Concentration
Platelet Count
Red Blood Cell Morphology
Reticulocyte Count (Absolute)
Packed Cell Volume

b. Serum Chemistry

Albumin
Globulin
Albumin/Globulin (A/G) Ratio
Urea Nitrogen
Glucose
Alkaline Phosphatase
Bilirubin
Creatine Kinase (CK)
Total Bile Acids (TBA)
Sorbitol Dehydrogenase (SDH)
Aspartate Aminotransferase (AST)
Alanine Aminotransferase (ALT)
Sodium
Total Protein
Potassium
Chloride
Creatinine
Cholesterol
Phosphorous (PO4)

c. Urinalysis: The following parameters will be evaluated: urine volume, levels of sodium and potassium, color, appearance, refractive index, specific gravity, microscopic evaluation, and qualitative measurement of glucose, urobilinogen, pH, protein, ketones, blood, nitrites, leukocytes, creatinine and bilirubin.

15. Acetylcholinesterase Inhibition: Blood samples for AChE will be collected at two intervals on the second day of dosing (at least 2 hours after dosing) and at the end of the study (during week 4 of treatment). Blood samples will be collected via the retroorbital sinus while the animal is properly anesthetized (i.e., 70% CO_2/30% air).

16. Postmortem Procedures:

a. Gross Necropsy: All rats, including those dying spontaneously during the study or sacrificed *in extremis*, will be subjected to an extensive necropsy. Upon the discretion of the Sponsor Representative, a gross necropsy may be performed on all early deaths (e.g.; less than two days of exposure) rather than a complete necropsy. However, any tissues with suspect lesions will be collected. The Sponsor will be consulted to determine if these tissues will be processed and examined by the pathologist. At study termination, rats will be euthanized using sodium pentobarbital overdose, bled and necropsied. Organs listed below will be collected and weighed, as described under section 16.b. The presence of lesions or other abnormal conditions will be noted and described for the study record.

b. Tissue Collection: Bone marrow smears and the tissues listed below will be collected from all animals. In addition, tissues marked with an asterisk from all rats will be removed, trimmed of excess adherent fat and wet tissue weights will be measured. All tissues (excluding those in brackets) from the vehicle control and highest surviving dose group will be sectioned and examined. Tissues in brackets will be examined if gross signs of toxicity/target organ involvement is observed. Examination of other tissues from the remaining groups will be done if necessary to determine a no-effect-level of compound-related tissue changes found in the high dose group following consultation with the Sponsor and at additional cost to the Sponsor.

[Eyes]
Brain*
Pituitary
Lung
Thymus
Heart*
Aorta
Thyroid/parathyroid
Esophagus
Trachea
Liver*
Kidneys*
Adrenal glands*
Spleen*
Pancreas
Salivary glands
Submandibular lymph nodes
[Skeletal muscle]
Bone marrow (sternebrae)
Testes*
[Epididymis]
[Seminal vesicle]
[Prostate]
Ovaries*
Uterus
Stomach
Duodenum
Jejunum
Ileum
Cecum
Colon
Rectum
Urinary bladder
Mesenteric lymph nodes
[Spinal cord-thoracic, cervical, lumbar]
[Mammary gland]
Sciatic nerve
[Femur]
Skin (Application Site and Untreated)
[Exorbital lacrimal gland]
[Zymbal gland]
Any other gross lesion
Ear tag

Tissue masses, suspect lesions and associated regional lymph nodes will also be collected if present. The tissue samples collected will be sliced into appropriate-sized sections and fixed in 10% neutral buffered formalin. Tissues will be prepared for microscopic examination by a pathologist.

c. Evaluation of Acetylcholinesterase Activity: AChE activity in red blood cell and plasma will be quantitated. All procedures to determine the AChE activity (Ellmen *et al.*, 1961) will be described in the raw data.

17. Statistical Analysis:

Body weight, food consumption, clinical pathology (clinical chemistry and hematology), absolute organ weights and relative organ-to-body weight will be analyzed separately by sex using an analysis of variance (ANOVA). A minimum significance of $p \leq 0.05$ will be used in all comparisons. All parameters described above as well as mortality and necropsy data will be tabulated. The results will be presented in a formal written report. AChE activity will be performed using analysis of variance, with post-hoc comparisons made using Dunnett's test. A minimum significance level of $p \leq 0.05$ will be used for all comparisons.

18. Raw Data Notebooks:

a. Contents: All original data will be maintained in study notebooks. These will include but not necessarily be limited to the following:

(1) The original signed protocol with any protocol amendments/deviations.
(2) Test substance characterization and preparation records.
(3) Animal purchasing and receiving records and randomization procedures.
(4) Body weights.
(5) Food consumption.
(6) Daily moribundity/mortality records.
(7) Observations.
(8) Physical examinations.
(9) Necropsy sheets.
(10) AChE assay data.

b. Storage: All original data (*i.e.*, data generated at IITRI), specimens and a copy of the final report will be retained in the IITRI archives for 5 years after the submission of the signed final report. At that time, the Sponsor will be contacted in order to determine the final disposition of the archival materials and will be responsible for all costs associated with continued storage of the archival materials in the IITRI archives or for the shipment of these materials to a new storage facility. IITRI's Quality Assurance Unit will maintain a complete record of the disposition of all archival materials.

19. Reports: One copy of a draft report will be submitted to the Sponsor for review. After receipt and review of the Sponsor's comments, appropriate changes will be made and two copies of a signed Final Report will be provided to the Sponsor.

20. Personnel: **Curriculum vitae** for all personnel involved in the execution of the study are on file at IITRI.

21. GLP Compliance:

    This study will be conducted in compliance with EPA Good Laboratory Practice Standards (40 CFR Part 792).

22. Quality Assurance Monitoring:

    The Quality Assurance Unit will audit the protocol and all reports, and will monitor the facilities, equipment, personnel, methods, practices, records, and controls used in this study to assure that they are in conformance with this protocol, company SOPs, and the appropriate Good Laboratory Practice regulations. The QAU will inspect at least one in-life phase of the study.

23. Animal Welfare Compliance Statement:

    This study will comply with all applicable sections of the Animal Welfare Act (Title 9, Code of Federal Regulations), the Public Health Service Policy on Humane Care and Use of Laboratory Animals (NIH Office of Protection from Research Risks, 1986), and the Guide for the Care and Use of Laboratory Animals (1996). The Sponsor's signature on the study protocol documents for the Study Director the Sponsor's assurance that the study described in this protocol does not unnecessarily duplicate previous experiments, and that no known acceptable non-animal alternatives were available. Wherever possible, procedures used in this study have been designed to avoid or minimize discomfort, distress, and pain to animals. All methods to be used are described in this study protocol or in written laboratory standard operating procedures.

24. Changes of the Protocol:

    No changes of the protocol will be made without the consent of the Sponsor. All changes to the protocol will be signed and dated by the Study Director and maintained with the protocol. In the event that the Sponsor authorizes a protocol change verbally, the change will be honored by IITRI and will be documented by a protocol amendment.

25. Humane Treatment Statement:

    The Institutional Animal Care and Use Committee at IITRI has reviewed this protocol and deems its study design appropriate to meet the objectives of the study, while minimizing both pain and distress to the test animals. If anesthetic, analgesic, or tranquilizer drugs can be used, they are the proper type for the given species. If euthanasia is to be performed, the method is proper for the given species.

Appendix A

PROTOCOL AMENDMENT

IITRI Project No. 1052

Study No. 3

Protocol Amendment No.: 1

Study Title: Four-Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats

1. Section: 11. Experimental Design

Effective May 28, 1999, the 5% sodium hydroxide (Positive Control Group) will no longer be dosed and the animals will be euthanized and discarded without necropsy.

Reason: Dosing was ceased due to the severe skin reaction noted in the Positive Control rats. No deaths and no signs of systemic toxicity were evident in this group, therefore it was decided to remove these animals from the study.

2. Section: 14.b. Clinical Pathology, Serum Chemistry

Effective May 21, 1999, calcium and triglycerides will be measured at the termination of the study.

Reason: These parameters were inadvertently omitted from the protocol.

3. Section: 16.a. Postmortem Procedures, Gross Necropsy

Effective May 21, 1999, all High Dose (5% TMAH) animals will receive a gross necropsy. However, any tissues with suspect lesions will be collected. A complete necropsy will be performed on the Mid-High Dose (3%) and any animal from the other dose groups that survive at least two days of TMAH exposure.

Reason: It is unlikely that tissues harvested from rats dying from acute toxicity would provide any valuable microscopic evidence for the observed toxicity.

John C. Findlay 6/9/99

John C. Findlay, B.S. Date
Study Director

Bernadette Ryan 6/9/99

Bernadette Ryan, Ph.D., D.A.B.T. Date
Manager, Regulatory Toxicology Division

6/14/99

Bradford Brooks, Ph.D. Date
Sponsor Representative

Appendix A

PROTOCOL AMENDMENT

IITRI Project No. 1052

Study No. 3

Protocol Amendment No.: 2

Study Title: Four-Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats

Section: 11. Experimental Design:

Effective June 17, 1999, three additional groups will be added to the study. The groups will be composed of 6 rats/sex/group. Two of the groups will be dermally exposed to the test substance at 5 and 25% TMAH. The third group will serve as a vehicle control and will be exposed to DI water. Approximately 1-3 hours after treatment initiation or at peak observation of clinical signs, blood will be collected via the abdominal aorta from animals anesthized with sodium pentobarbitol for blood gas analysis including pO_2, pCO_2, pH, and HCO_3 (bicarbonate, derived). Hematology parameters will also be measured. Samples for blood gas analysis will be held on ice and analyzed within approximately 2 hours of collection. Animals will be discarded without necropsy.

Reason: The Sponsor Representative requested these parameters in an attempt to determine the possible cause of death.

John C. Findlay 6/23/99

John C. Findlay, B.S. Date
Study Director

Bernadette Ryan 6/23/99

Bernadette Ryan, Ph.D., D.A.B.T. Date
Manager, Regulatory Toxicology Division

Bradford O. Brooks 6/25/99

Bradford Brooks, Ph.D. Date
Sponsor Representative

PROTOCOL AMENDMENT

IITRI Project No. 1052

Study No. 3

Protocol Amendment No.: 3

Study Title: Four-Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats

Section: 16.b. Postmortem Procedures: Tissue Collection:

Effective June 25, 1999, all tissues listed in the protocol (excluding those in brackets) from the 1% TMAH dose group in addition to the 3% dose (i.e.; highest surviving group) and vehicle control group will be sectioned and examined.

Reason: The Sponsor Representative requested the additional dose group for processing.

John C. Findlay 7/6/99

John C. Findlay, B.S. Date
Study Director

Bernadette Ryan 7/6/99

Bernadette Ryan, Ph.D., D.A.B.T. Date
Manager, Regulatory Toxicology Division

Bradford Brooks 7/12/99

Bradford Brooks, Ph.D. Date
Sponsor Representative

PROTOCOL AMENDMENT

IITRI Project No. 1052

Study No. 3

Protocol Amendment No.: 4

Study Title: Four-Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats

Section: 16.b. Postmorten Procedures: Tissue Collection:

Effective July 28, 1999, all skin (application site) in the 0.25 and 0.55% dose groups will be sectioned and examined.

Reason: The study pathologist recommended the additional dose groups based on his findings in the 5 and 3% dose groups.

John C. Findlay 8/2/99

John C. Findlay, B.S. Date
Study Director

Bernadette Ryan 8/2/99

Bernadette Ryan, Ph.D., D.A. B.T. Date
Manager, Regulatory Toxicology Division

Bradford D. Brooks 8/3/99

Bradford Brooks, Ph.D. Date
Sponsor Representative

Appendix B: Analytical Chemistry Report

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Appendix B - Analytical Chemistry

The concentration of TMAH in water formulations was determined by titration using HCl. Aliquots of dosing formulations were diluted in water and titrated to the equivalence point with dilute HCl.

Standards were prepared by accurately weighing aliquots of the neat test article into volumetric flasks, then diluting to volume with water.

Calibration was performed by titrating each standard with dilute HCl (0.008M) and determining the volume (in milliliters of titrant) required for reaching the equivalence point (pH 7). A calibration curve was constructed which related the known concentration (based on preparation) versus the titrant volume (in ml). The calibration was linear (Analytical Chemistry Table 1).

Stability of the water formulations was verified by reanalysis of a 0.25% and a 5% solution after storage at room temperature for up to 13 days. Solutions were analyzed after 0, 8 and 13 days of storage. Both solutions were still stable after 13 days (Analytical Chemistry Table 2).

Formulations used during the study were prepared weekly and analyzed twice. The results of the individual analyses are contained in Analytical Chemistry Table 3. The average percent analytical/theoretical concentration was 101.0%, 102.1%, 100.3%, 100.0% and 100.4% for the 0.25%, 0.55%, 1%, 3% and 5% solutions, respectively. The analyzed concentration was within 3 percent of the theoretical concentration for every dosing solution. TMAH was not detected in any control group sample.

The positive control (5% sodium hydroxide) was also analyzed using the same titration procedure. The formulation used for the study was analyzed at 4.964% (mean of duplicate titrations) and was stable for at least 8 days.

Scott Garthwaite 5-4-00

Scott Garthwaite, B.S. Date
Analytical Chemist
Life Sciences Operation

Appendix B - Analytical Chemistry

Table 1
Calibration

Concentration (mg/ml)	ml titrant
0.2025	13.4
0.2025	13.5
0.2267	15.0
0.2267	14.8
0.2518	16.5
0.2518	16.7
0.2785	18.2
0.2785	18.3
0.3031	20.3
0.3031	20.3
Slope	67.391
Y-intercept	-0.3176
Correlation Coefficient	0.996

Appendix B - Analytical Chemistry

Table 2
Stability of Dosing Formulations

Date of Analysis	Days of Storage	0.25% solution		5% solution	
		Analyzed Concentration (%)	Percent of Original Analysis	Analyzed Concentration (%)	Percent of Original Analysis
5-25-99	0[1]	0.2525	-	5.006	-
6-2-99	8[1]	0.2562	101.5	5.036	100.6
6-7-99	13[1]	0.2570	101.8	5.110	102.1

[1] These solutions were prepared on 5-25-99 and stored at room temperature.

Appendix B - Analytical Chemistry

Table 3
Dosing Solution Analyses

Theoretical Concentration	Analytical Concentration (%)[1]			Analytical/Theoretical Concentration (%)
	Week 1	Week 2	Mean	
0%	BDL[2]	BDL	BDL	-
0.25%	0.2525	0.2525	0.2525	101.0
0.55%	0.5659	0.5570	0.5615	102.1
1%	0.9903	1.015	1.003	100.3
3%	2.990	3.008	2.999	100.0
5%	5.006	5.036	5.021	100.4

[1] Reported concentrations are means of two replicate analyses
[2] BDL = below detection limit

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 1-M SEX: MALE
WEEK 0-WEEK 4 DOSE: 0 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
336	Poss. grooming irritation			WEEK 4	WEEK 4	1
	Normal			WEEK 0	WEEK 4	5
337	Normal			WEEK 0	WEEK 4	6
338	Normal			WEEK 0	WEEK 4	6
339	Normal			WEEK 0	WEEK 4	6
340	Normal			WEEK 0	WEEK 4	6
341	Normal			WEEK 0	WEEK 4	6
342	Normal			WEEK 0	WEEK 4	6
343	Redness around nose fur			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 4	5
344	Lesion - scabbed			WEEK 1	WEEK 2	2
	Normal			WEEK 0	WEEK 4	4
345	Poss. grooming irritation			WEEK 4	WEEK 4	1
	Normal			WEEK 0	WEEK 4	5

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 2-M SEX: MALE
WEEK 0-WEEK 4 DOSE: 2.5 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
356	Normal			WEEK 0	WEEK 4	6
357	Normal			WEEK 0	WEEK 4	6
358	Normal			WEEK 0	WEEK 4	6
359	Normal			WEEK 0	WEEK 4	6
360	Normal			WEEK 0	WEEK 4	6
361	Irritable			WEEK 4	WEEK 4	1
	Normal			WEEK 0	WEEK 4	5
362	Redness around the eyes			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 4	5
363	Redness around nose fur			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 4	5
364	Normal			WEEK 0	WEEK 4	6
365	Normal			WEEK 0	WEEK 4	6

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 3-M SEX: MALE
WEEK 0-WEEK 4 DOSE: 5.5(mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
376	Poss. grooming irritation			WEEK 3	WEEK 3	1
	Normal			WEEK 0	WEEK 4	5
377	Normal			WEEK 0	WEEK 4	6
378	Poss. grooming irritation			WEEK 4	WEEK 4	2
	Normal			WEEK 0	WEEK 3	4
379	Redness around the eyes			WEEK 3	WEEK 4	3
	Normal			WEEK 0	WEEK 2	3
380	Normal			WEEK 0	WEEK 4	6
381	Lesion - scabbed			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 4	5
382	Normal			WEEK 0	WEEK 4	6
383	Lesion - scabbed			WEEK 2	WEEK 2	1
	Poss. grooming irritation			WEEK 3	WEEK 3	1
	Normal			WEEK 0	WEEK 4	4
384	Normal			WEEK 0	WEEK 4	6
385	Normal			WEEK 0	WEEK 4	6

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 4-M SEX: MALE
WEEK 0-WEEK 4 DOSE: 10 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
396	Redness around nose fur			WEEK 1	WEEK 1	1
	Lesion - scabbed			WEEK 2	WEEK 4	3
	Normal			WEEK 0	WEEK 4	2
397	Lesion - scabbed			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 4	5
398	Lesion - scabbed			WEEK 2	WEEK 4	4
	Normal			WEEK 0	WEEK 1	2
399	Normal			WEEK 0	WEEK 4	6
400	Lesion - scabbed			WEEK 4	WEEK 4	2
	Poss. grooming irritation			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 3	3
401	Lesion - scabbed			WEEK 2	WEEK 4	4
	Normal			WEEK 0	WEEK 1	2
402	Lesion - scabbed			WEEK 2	WEEK 4	4
	Normal			WEEK 0	WEEK 1	2
403	Lesion - scabbed			WEEK 2	WEEK 4	4
	Normal			WEEK 0	WEEK 1	2
404	Lesion - scabbed			WEEK 2	WEEK 4	4
	Normal			WEEK 0	WEEK 1	2
405	Lesion - scabbed			WEEK 2	WEEK 3	2
	Poss. grooming irritation			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 4	3

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 5-M SEX: MALE
WEEK 0-WEEK 4 DOSE: 30 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC ONSET	DURATION	FREQUENCY
416	Animal found dead		WEEK 1	WEEK 1	1
	Poss. grooming irritation		WEEK 1	WEEK 1	1
	Normal		WEEK 0	WEEK 0	1
417	Animal found dead		WEEK 1	WEEK 1	1
	Poss. grooming irritation		WEEK 1	WEEK 1	1
	Normal		WEEK 0	WEEK 0	1
418	Animal found dead		WEEK 1	WEEK 1	1
	Lesion - scabbed		WEEK 1	WEEK 1	1
	Normal		WEEK 0	WEEK 0	1
419	Animal found dead		WEEK 1	WEEK 1	1
	Lesion - scabbed		WEEK 1	WEEK 1	1
	Normal		WEEK 0	WEEK 0	1
420	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1
421	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1
422	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1
423	Lesion - scabbed		WEEK 1	WEEK 4	5
	Redness around the eyes		WEEK 1	WEEK 1	1
	Normal		WEEK 0	WEEK 0	1
424	Animal found dead		WEEK 1	WEEK 1	1
	Poss. grooming irritation		WEEK 1	WEEK 1	1
	Normal		WEEK 0	WEEK 0	1
425	Lesion - scabbed		WEEK 1	WEEK 4	5
	Normal		WEEK 0	WEEK 0	1

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3
WEEK 0-WEEK 4
GROUP: 6-M
DOSE: 50 (mg/kg)
SEX: MALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
436	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
437	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
438	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
439	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
440	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
441	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
442	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
443	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
444	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
445	Animal found dead			WEEK 1	WEEK 1	1
	Lesion - scabbed			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 7-M SEX: MALE
WEEK 0-WEEK 4 DOSE: 50(mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
456	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
457	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
458	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
459	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
460	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
461	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
462	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
463	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
464	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1
465	Eschar			WEEK 1	WEEK 2	2
	Terminal Sacrifice			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 0	1

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 1-F SEX: FEMALE
WEEK 0-WEEK 4 DOSE: 0 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
346	Normal			WEEK 0	WEEK 4	6
347	Poss. grooming irritation			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 4	5
348	Normal			WEEK 0	WEEK 4	6
349	Poss. grooming irritation			WEEK 3	WEEK 4	2
	Normal			WEEK 0	WEEK 4	4
350	Normal			WEEK 0	WEEK 4	6
351	Normal			WEEK 0	WEEK 4	6
352	Normal			WEEK 0	WEEK 4	6
353	Poss. grooming irritation			WEEK 4	WEEK 4	1
	Normal			WEEK 0	WEEK 4	5
354	Normal			WEEK 0	WEEK 4	6
355	Normal			WEEK 0	WEEK 4	6

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 2-F SEX: FEMALE
WEEK 0-WEEK 4 DOSE: 2.5(mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
366	Normal			WEEK 0	WEEK 4	6
367	Normal			WEEK 0	WEEK 4	6
368	Poss. grooming irritation			WEEK 4	WEEK 4	1
	Normal			WEEK 0	WEEK 4	5
369	Poss. grooming irritation			WEEK 4	WEEK 4	2
	Normal			WEEK 0	WEEK 3	4
370	Normal			WEEK 0	WEEK 4	6
371	Normal			WEEK 0	WEEK 4	6
372	Normal			WEEK 0	WEEK 4	6
373	Normal			WEEK 0	WEEK 4	6
374	Normal			WEEK 0	WEEK 4	6
375	Normal			WEEK 0	WEEK 4	6

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 3-F SEX: FEMALE
WEEK 0-WEEK 4 DOSE: 5.5(mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
386	Poss. grooming irritation			WEEK 3	WEEK 4	3
	Normal			WEEK 0	WEEK 2	3
387	Normal			WEEK 0	WEEK 4	6
388	Poss. grooming irritation			WEEK 3	WEEK 3	1
	Lacrimation			WEEK 2	WEEK 2	1
	Normal			WEEK 0	WEEK 4	4
389	Normal			WEEK 0	WEEK 4	6
390	Lesion - scabbed			WEEK 3	WEEK 4	3
	Normal			WEEK 0	WEEK 2	3
391	Normal			WEEK 0	WEEK 4	6
392	Lesion - scabbed			WEEK 3	WEEK 4	3
	Normal			WEEK 0	WEEK 2	3
393	Poss. grooming irritation			WEEK 4	WEEK 4	1
	Normal			WEEK 0	WEEK 4	5
394	Normal			WEEK 0	WEEK 4	6
395	Lesion - scabbed			WEEK 3	WEEK 3	1
	Normal			WEEK 0	WEEK 4	5

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 4-F SEX: FEMALE
WEEK 0-WEEK 4 DOSE: 10 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
406	Lesion - scabbed			WEEK 2	WEEK 4	4
	Normal			WEEK 0	WEEK 1	2
407	Lesion - scabbed			WEEK 3	WEEK 4	3
	Normal			WEEK 0	WEEK 2	3
408	Lesion - scabbed			WEEK 2	WEEK 4	4
	Normal			WEEK 0	WEEK 1	2
409	Lesion - scabbed			WEEK 3	WEEK 3	1
	Poss. grooming irritation			WEEK 4	WEEK 4	2
	Normal			WEEK 0	WEEK 2	3
410	Lesion - scabbed			WEEK 3	WEEK 4	3
	Normal			WEEK 0	WEEK 2	3
411	Lesion - scabbed			WEEK 2	WEEK 3	2
	Poss. grooming irritation			WEEK 4	WEEK 4	2
	Normal			WEEK 0	WEEK 1	2
412	Lesion - scabbed			WEEK 3	WEEK 4	3
	Normal			WEEK 0	WEEK 2	3
413	Lesion - scabbed			WEEK 3	WEEK 3	1
	Normal			WEEK 0	WEEK 4	5
414	Lesion - scabbed			WEEK 3	WEEK 3	1
	Poss. grooming irritation			WEEK 4	WEEK 4	2
	Normal			WEEK 0	WEEK 2	3
415	Lesion - scabbed			WEEK 2	WEEK 3	2
	Normal			WEEK 0	WEEK 4	4

Appendix C

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3
WEEK 0-WEEK 4

GROUP: 5-F
DOSE: 30 (mg/kg)

SEX: FEMALE

ANIMAL #	OBSERVATIONS	SEVERITY	LOC ONSET	DURATION	FREQUENCY
426	Lesion - scabbed		WEEK 1	WEEK 4	5
	Normal		WEEK 0	WEEK 0	1
427	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1
428	Animal found dead		WEEK 1	WEEK 1	1
	Lesion - scabbed		WEEK 1	WEEK 1	1
	Normal		WEEK 0	WEEK 0	1
429	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1
430	Animal found dead		WEEK 2	WEEK 2	1
	Lesion - scabbed		WEEK 1	WEEK 2	2
	Normal		WEEK 0	WEEK 0	1
431	Animal found dead		WEEK 2	WEEK 2	1
	Lesion - scabbed		WEEK 1	WEEK 2	2
	Normal		WEEK 0	WEEK 0	1
432	Lesion - scabbed		WEEK 1	WEEK 4	5
	Normal		WEEK 0	WEEK 0	1
433	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1
434	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1
435	Animal found dead		WEEK 0	WEEK 0	1
	Normal		WEEK 0	WEEK 0	1

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 6-F SEX: FEMALE
WEEK 0-WEEK 4 DOSE: 50(mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
446	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
447	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
448	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
449	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
450	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
451	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
452	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
453	Animal found dead			WEEK 1	WEEK 1	1
	Lesion - scabbed			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
454	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1
455	Animal found dead			WEEK 0	WEEK 0	1
	Normal			WEEK 0	WEEK 0	1

INDIVIDUAL CLINICAL SIGNS

STUDY: 1052SN3 GROUP: 7-F SEX: FEMALE
WEEK 0-WEEK 4 DOSE: 50 (mg/kg)

ANIMAL #	OBSERVATIONS	SEVERITY	LOC	ONSET	DURATION	FREQUENCY
466	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
467	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
468	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
469	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
470	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
471	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
472	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
473	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
474	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1
475	Eschar			WEEK 1	WEEK 1	1
	Terminal Sacrifice			WEEK 1	WEEK 1	1
	Normal			WEEK 0	WEEK 0	1

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 1-M SEX: MALE
DOSE: 0 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
336	232	276	310	348	365
337	224	266	298	330	343
338	222	259	301	344	369
339	219	253	283	319	345
340	231	276	309	351	376
341	228	270	294	326	344
342	232	258	286	318	342
343	216	250	293	334	352
344	219	263	298	338	365
345	231	275	315	352	374
MEAN	225	265	299	336	358
S.D.	6.2	9.6	10.4	12.7	13.7
N	10	10	10	10	10

--: Data Unavailable

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 2-M SEX: MALE
DOSE: 2.5 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
356	226	263	303	334	355
357	231	263	288	329	349
358	234	258	281	296	319
359	212	246	273	305	327
360	218	259	293	335	360
361	216	254	291	333	357
362	233	271	306	341	363
363	216	257	279	318	336
364	220	261	296	336	361
365	220	264	297	327	348
MEAN	223	260	291	325	348
S.D.	7.8	6.7	10.6	14.6	15.2
N	10	10	10	10	10

--: Data Unavailable

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 3-M SEX: MALE
DOSE: 5.5 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
376	220	263	296	330	355
377	221	261	295	335	351
378	240	281	319	362	402
379	228	265	299	341	356
380	215	250	281	319	344
381	236	270	294	330	362
382	219	255	288	330	358
383	239	280	310	346	369
384	216	251	282	323	349
385	226	263	286	314	330
MEAN	226	264	295	333	358
S.D.	9.4	10.7	12.1	14.0	18.8
N	10	10	10	10	10

--: Data Unavailable

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 4-M SEX: MALE
DOSE: 10 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
396	221	254	278	302	320
397	225	263	295	335	371
398	216	246	280	313	334
399	206	248	278	313	333
400	245	285	315	359	381
401	230	269	302	342	370
402	218	246	280	311	333
403	212	247	283	321	342
404	228	272	305	337	362
405	229	274	306	333	351
MEAN	223	260	292	327	350
S.D.	11.0	14.1	14.0	17.5	20.4
N	10	10	10	10	10

--: Data Unavailable

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 5-M SEX: MALE
DOSE: 30 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
416	227	278	a	a	a
417	213	260	a	a	a
418	235	263	a	a	a
419	235	278	a	a	a
420	209	a	a	a	a
421	227	a	a	a	a
422	209	a	a	a	a
423	223	259	283	321	348
424	231	276	a	a	a
425	236	281	299	344	374
MEAN	225	271	291	333	361
S.D.	10.7	9.6	11.3	16.3	18.4
N	10	7	2	2	2

--: Data Unavailable a: Animal found dead

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 6-M SEX: MALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
436	231	a	a	a	a
437	226	a	a	a	a
438	247	a	a	a	a
439	217	a	a	a	a
440	219	a	a	a	a
441	214	a	a	a	a
442	236	a	a	a	a
443	225	a	a	a	a
444	227	a	a	a	a
445	217	256	a	a	a
MEAN	226	256	--	--	--
S.D.	10.1	--	--	--	--
N	10	1	0	0	0

--: Data Unavailable a: Animal found dead

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 7-M SEX: MALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
456	222	262	310	e	e
457	214	254	309	e	e
458	215	259	313	e	e
459	223	254	313	e	e
460	234	271	304	e	e
461	225	270	331	e	e
462	229	261	310	e	e
463	223	257	298	e	e
464	210	242	285	e	e
465	226	263	307	e	e
MEAN	222	259	308	--	--
S.D.	7.3	8.4	11.7	--	--
N	10	10	10	0	0

--: Data Unavailable e: Terminal Sacrifice

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
346	153	169	195	210	233
347	157	167	188	203	213
348	158	170	192	208	215
349	169	183	205	230	243
350	176	191	208	229	231
351	158	173	197	210	225
352	169	182	205	227	233
353	171	203	248	245	267
354	158	172	197	217	232
355	154	157	179	192	216
MEAN	162	177	201	217	231
S.D.	8.1	13.3	18.5	15.6	16.0
N	10	10	10	10	10

--: Data Unavailable

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 2-F SEX: FEMALE
DOSE: 2.5 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
366	165	184	202	224	235
367	162	167	192	209	227
368	178	190	211	229	240
369	159	180	208	233	246
370	154	174	194	215	224
371	155	167	192	205	223
372	167	186	207	233	253
373	170	184	201	219	227
374	148	164	187	202	211
375	155	164	182	190	208
MEAN	161	176	198	216	229
S.D.	8.9	10.0	9.7	14.4	14.4
N	10	10	10	10	10

--: Data Unavailable

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 3-F SEX: FEMALE
DOSE: 5.5 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
386	158	180	197	213	232
387	153	171	188	203	215
388	161	179	194	228	229
389	175	194	220	237	244
390	158	181	207	225	233
391	170	189	214	236	248
392	174	190	214	237	241
393	154	171	187	196	206
394	154	164	183	202	208
395	155	180	203	223	239
MEAN	161	180	201	220	230
S.D.	8.6	9.4	12.9	15.5	15.0
N	10	10	10	10	10

--: Data Unavailable

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 4-F SEX: FEMALE
DOSE: 10 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
406	162	192	224	225	245
407	174	190	214	235	248
408	151	176	212	245	240
409	172	200	224	247	260
410	153	172	191	222	237
411	152	167	185	195	202
412	158	165	188	204	224
413	174	182	216	239	249
414	156	171	188	207	216
415	165	180	204	219	233
MEAN	162	180	205	224	235
S.D.	9.1	11.5	15.4	17.9	17.3
N	10	10	10	10	10

--: Data Unavailable

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 5-F SEX: FEMALE
DOSE: 30 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
426	173	194	217	242	251
427	155	a	a	a	a
428	148	157	a	a	a
429	166	a	a	a	a
430	160	169	193	a	a
431	165	174	183	a	a
432	173	190	214	236	249
433	152	a	a	a	a
434	163	a	a	a	a
435	160	a	a	a	a
MEAN	162	177	202	239	250
S.D.	8.3	15.3	16.4	4.2	1.4
N	10	5	4	2	2

--: Data Unavailable a: Animal found dead

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 6-F SEX: FEMALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
446	158	a	a	a	a
447	162	a	a	a	a
448	170	a	a	a	a
449	155	a	a	a	a
450	174	a	a	a	a
451	167	a	a	a	a
452	153	a	a	a	a
453	148	160	a	a	a
454	156	a	a	a	a
455	164	a	a	a	a
MEAN	161	160	--	--	--
S.D.	8.2	--	--	--	--
N	10	1	0	0	0

--: Data Unavailable a: Animal found dead

Appendix D

INDIVIDUAL BODY WEIGHTS (Grams)

STUDY: 1052SN3 GROUP: 7-F SEX: FEMALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 0	WEEK 1	WEEK 2	WEEK 3	WEEK 4
466	150	177	e	e	e
467	159	167	e	e	e
468	154	189	e	e	e
469	154	171	e	e	e
470	171	200	e	e	e
471	165	182	e	e	e
472	164	202	e	e	e
473	177	198	e	e	e
474	170	188	e	e	e
475	160	184	e	e	e
MEAN	162	186	--	--	--
S.D.	8.6	12.0	--	--	--
N	10	10	0	0	0

--: Data Unavailable e: Terminal Sacrifice

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 1-M SEX: MALE
DOSE: 0 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
336	44	34	38	17	133
337	42	32	32	13	119
338	37	42	43	25	147
339	34	30	36	26	126
340	45	33	42	25	145
341	42	24	32	18	116
342	26	28	32	24	110
343	34	43	41	18	136
344	44	35	40	27	146
345	44	40	37	22	143
MEAN	39	34	37	22	132
S.D.	6.3	6.1	4.2	4.7	13.6
N	10	10	10	10	10

--: Data Unavailable

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 2-M SEX: MALE
DOSE: 2.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
356	37	40	31	21	129
357	32	25	41	20	118
358	24	23	15	23	85
359	34	27	32	22	115
360	41	34	42	25	142
361	38	37	42	24	141
362	38	35	35	22	130
363	41	22	39	18	120
364	41	35	40	25	141
365	44	33	30	21	128
MEAN	37	31	35	22	125
S.D.	5.8	6.3	8.3	2.2	17.1
N	10	10	10	10	10

--: Data Unavailable

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 3-M SEX: MALE
DOSE: 5.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
376	43	33	34	25	135
377	40	34	40	16	130
378	41	38	43	40	162
379	37	34	42	15	128
380	35	31	38	25	129
381	34	24	36	32	126
382	36	33	42	28	139
383	41	30	36	23	130
384	35	31	41	26	133
385	37	23	28	16	104
MEAN	38	31	38	25	132
S.D.	3.1	4.6	4.6	7.8	14.2
N	10	10	10	10	10

--: Data Unavailable

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 4-M SEX: MALE
DOSE: 10 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
396	33	24	24	18	99
397	38	32	40	36	146
398	30	34	33	21	118
399	42	30	35	20	127
400	40	30	44	22	136
401	39	33	40	28	140
402	28	34	31	22	115
403	35	36	38	21	130
404	44	33	32	25	134
405	45	32	27	18	122
MEAN	37	32	34	23	127
S.D.	5.8	3.3	6.2	5.4	13.8
N	10	10	10	10	10

--: Data Unavailable

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 5-M SEX: MALE
DOSE: 30 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
416	51	a	a	a	--
417	47	a	a	a	--
418	28	a	a	a	--
419	43	a	a	a	--
420	a	a	a	a	--
421	a	a	a	a	--
422	a	a	a	a	--
423	36	24	38	27	125
424	45	a	a	a	--
425	45	18	45	30	138
MEAN	42	21	42	29	132
S.D.	7.7	4.2	4.9	2.1	9.2
N	7	2	2	2	2

--: Data Unavailable a: Animal found dead

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 6-M SEX: MALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
436	a	a	a	a	--
437	a	a	a	a	--
438	a	a	a	a	--
439	a	a	a	a	--
440	a	a	a	a	--
441	a	a	a	a	--
442	a	a	a	a	--
443	a	a	a	a	--
444	a	a	a	a	--
445	39	a	a	a	--
MEAN	39	--	--	--	--
S.D.	--	--	--	--	--
N	1	0	0	0	0

--: Data Unavailable a: Animal found dead

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 7-M SEX: MALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
456	40	48	e	e	--
457	40	55	e	e	--
458	44	54	e	e	--
459	31	59	e	e	--
460	37	33	e	e	--
461	45	61	e	e	--
462	32	49	e	e	--
463	34	41	e	e	--
464	32	43	e	e	--
465	37	44	e	e	--
MEAN	37	49	--	--	--
S.D.	5.0	8.7	--	--	--
N	10	10	0	0	0

--: Data Unavailable e: Terminal Sacrifice

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
346	16	26	15	23	80
347	10	21	15	10	56
348	12	22	16	7	57
349	14	22	25	13	74
350	15	17	21	2	55
351	15	24	13	15	67
352	13	23	22	6	64
353	32	45	-3	22	96
354	14	25	20	15	74
355	3	22	13	24	62
MEAN	14	25	16	14	69
S.D.	7.2	7.5	7.7	7.6	12.8
N	10	10	10	10	10

--: Data Unavailable

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 2-F SEX: FEMALE
DOSE: 2.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
366	19	18	22	11	70
367	5	25	17	18	65
368	12	21	18	11	62
369	21	28	25	13	87
370	20	20	21	9	70
371	12	25	13	18	68
372	19	21	26	20	86
373	14	17	18	8	57
374	16	23	15	9	63
375	9	18	8	18	53
MEAN	15	22	18	14	68
S.D.	5.3	3.6	5.5	4.6	11.1
N	10	10	10	10	10

--: Data Unavailable

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 3-F SEX: FEMALE
DOSE: 5.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
386	22	17	16	19	74
387	18	17	15	12	62
388	18	15	34	1	68
389	19	26	17	7	69
390	23	26	18	8	75
391	19	25	22	12	78
392	16	24	23	4	67
393	17	16	9	10	52
394	10	19	19	6	54
395	25	23	20	16	84
MEAN	19	21	19	10	68
S.D.	4.2	4.4	6.5	5.5	10.2
N	10	10	10	10	10

--: Data Unavailable

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 4-F SEX: FEMALE
DOSE: 10 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
406	30	32	1	20	83
407	16	24	21	13	74
408	25	36	33	-5	89
409	28	24	23	13	88
410	19	19	31	15	84
411	15	18	10	7	50
412	7	23	16	20	66
413	8	34	23	10	75
414	15	17	19	9	60
415	15	24	15	14	68
MEAN	18	25	19	12	74
S.D.	7.8	6.7	9.5	7.2	12.8
N	10	10	10	10	10

--: Data Unavailable

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 5-F SEX: FEMALE
DOSE: 30 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
426	21	23	25	9	78
427	a	a	a	a	--
428	9	a	a	a	--
429	a	a	a	a	--
430	9	24	a	a	--
431	9	9	a	a	--
432	17	24	22	13	76
433	a	a	a	a	--
434	a	a	a	a	--
435	a	a	a	a	--
MEAN	13	20	24	11	77
S.D.	5.7	7.3	2.1	2.8	1.4
N	5	4	2	2	2

--: Data Unavailable a: Animal found dead

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 6-F SEX: FEMALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
446	a	a	a	a	--
447	a	a	a	a	--
448	a	a	a	a	--
449	a	a	a	a	--
450	a	a	a	a	--
451	a	a	a	a	--
452	a	a	a	a	--
453	12	a	a	a	--
454	a	a	a	a	--
455	a	a	a	a	--
MEAN	12	--	--	--	--
S.D.	--	--	--	--	--
N	1	0	0	0	0

--: Data Unavailable a: Animal found dead

Appendix E

INDIVIDUAL WEIGHT GAIN (Grams)

STUDY: 1052SN3 GROUP: 7-F SEX: FEMALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4	TOTAL GAIN
466	27	e	e	e	--
467	8	e	e	e	--
468	35	e	e	e	--
469	17	e	e	e	--
470	29	e	e	e	--
471	17	e	e	e	--
472	38	e	e	e	--
473	21	e	e	e	--
474	18	e	e	e	--
475	24	e	e	e	--
MEAN	23	--	--	--	--
S.D.	9.1	--	--	--	--
N	10	0	0	0	0

--: Data Unavailable e: Terminal Sacrifice

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 1-M SEX: MALE
DOSE: 0 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
336	206	217	221	231
337	177	187	198	205
338	176	195	215	226
339	160	171	198	207
340	194	205	216	243
341	208	207	230	214
342	154	181	191	196
343	176	204	222	233
344	186	188	204	225
345	199	204	220	248
MEAN	184	196	212	223
S.D.	18.4	14.0	12.9	17.0
N	10	10	10	10

--: Data Unavailable

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 2-M SEX: MALE
DOSE: 2.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
356	176	193	--	219
357	178	183	198	211
358	174	178	189	197
359	178	178	204	230
360	177	200	231	234
361	180	198	217	231
362	177	189	222	233
363	189	181	196	198
364	189	206	241	257
365	209	206	230	239
MEAN	183	191	214	225
S.D.	10.6	11.0	18.2	18.8
N	10	10	9	10

--: Data Unavailable

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 3-M SEX: MALE
DOSE: 5.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
376	179	182	205	214
377	162	196	210	216
378	184	205	227	247
379	184	187	208	223
380	163	172	195	212
381	185	174	198	232
382	173	174	197	228
383	184	187	204	238
384	171	182	201	219
385	182	188	196	216
MEAN	177	185	204	225
S.D.	8.9	10.4	9.6	11.5
N	10	10	10	10

--: Data Unavailable

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 4-M SEX: MALE
DOSE: 10 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
396	192	176	188	198
397	191	207	220	246
398	177	188	225	239
399	167	178	189	215
400	180	206	235	247
401	183	195	209	247
402	158	170	186	214
403	157	191	188	204
404	194	209	223	239
405	196	203	208	225
MEAN	180	192	207	227
S.D.	14.6	14.1	18.3	18.7
N	10	10	10	10

--: Data Unavailable

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 5-M SEX: MALE
DOSE: 30 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
416	185	a	a	a
417	162	a	a	a
418	164	a	a	a
419	181	a	a	a
420	a	a	a	a
421	a	a	a	a
422	a	a	a	a
423	181	171	226	239
424	177	a	a	a
425	184	165	216	233
MEAN	176	168	221	236
S.D.	9.4	4.2	7.1	4.2
N	7	2	2	2

--: Data Unavailable a: Animal found dead

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 6-M SEX: MALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
436	a	a	a	a
437	a	a	a	a
438	a	a	a	a
439	a	a	a	a
440	a	a	a	a
441	a	a	a	a
442	a	a	a	a
443	a	a	a	a
444	a	a	a	a
445	185	a	a	a
MEAN	185	--	--	--
S.D.	--	--	--	--
N	1	0	0	0

--: Data Unavailable a: Animal found dead

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 7-M SEX: MALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
456	178	200	e	e
457	169	194	e	e
458	176	209	e	e
459	167	200	e	e
460	193	211	e	e
461	191	235	e	e
462	162	189	e	e
463	194	205	e	e
464	156	181	e	e
465	181	199	e	e
MEAN	177	202	--	--
S.D.	13.3	14.6	--	--
N	10	10	0	0

--: Data Unavailable e: Terminal Sacrifice

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 1-F SEX: FEMALE
DOSE: 0 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
346	147	156	164	182
347	123	150	167	164
348	133	175	196	192
349	146	162	189	182
350	149	166	172	160
351	137	158	163	168
352	146	148	166	168
353	158	204	172	191
354	154	173	198	189
355	140	160	171	188
MEAN	143	165	176	178
S.D.	10.3	16.2	13.3	12.2
N	10	10	10	10

--: Data Unavailable

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 2-F SEX: FEMALE
DOSE: 2.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
366	148	154	182	179
367	118	157	161	174
368	126	141	155	153
369	144	170	179	185
370	140	164	163	170
371	142	152	176	176
372	152	168	193	197
373	149	149	156	160
374	127	149	158	168
375	131	149	160	170
MEAN	138	155	168	173
S.D.	11.5	9.4	13.1	12.4
N	10	10	10	10

--: Data Unavailable

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 3-F SEX: FEMALE
DOSE: 5.5 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
386	134	138	154	160
387	129	141	165	154
388	142	146	175	145
389	158	183	196	190
390	132	151	165	166
391	129	151	158	167
392	148	165	175	180
393	148	154	175	175
394	141	143	165	163
395	154	174	183	187
MEAN	142	155	171	169
S.D.	10.4	14.9	12.4	14.3
N	10	10	10	10

--: Data Unavailable

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 4-F SEX: FEMALE
DOSE: 10 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
406	161	179	171	185
407	133	154	156	161
408	148	167	197	174
409	155	164	181	180
410	140	148	175	175
411	125	132	137	144
412	126	162	167	172
413	125	163	174	174
414	135	139	154	158
415	140	150	155	165
MEAN	139	156	167	169
S.D.	12.6	14.0	16.9	12.0
N	10	10	10	10

--: Data Unavailable

Appendix F

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 5-F SEX: FEMALE
DOSE: 30 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
426	144	178	189	194
427	a	a	a	a
428	158	a	a	a
429	a	a	a	a
430	140	163	a	a
431	123	138	a	a
432	151	161	183	189
433	a	a	a	a
434	a	a	a	a
435	a	a	a	a
MEAN	143	160	186	192
S.D.	13.2	16.5	4.2	3.5
N	5	4	2	2

--: Data Unavailable a: Animal found dead

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 6-F SEX: FEMALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
446	a	a	a	a
447	a	a	a	a
448	a	a	a	a
449	a	a	a	a
450	a	a	a	a
451	a	a	a	a
452	a	a	a	a
453	126	a	a	a
454	a	a	a	a
455	a	a	a	a
MEAN	126	--	--	--
S.D.	--	--	--	--
N	1	0	0	0

--: Data Unavailable a: Animal found dead

INDIVIDUAL FOOD CONSUMPTION (Grams)

STUDY: 1052SN3 GROUP: 7-F SEX: FEMALE
DOSE: 50 (mg/kg)

ANIMAL #	WEEK 1	WEEK 2	WEEK 3	WEEK 4
466	143	e	e	e
467	119	e	e	e
468	147	e	e	e
469	134	e	e	e
470	152	e	e	e
471	155	e	e	e
472	156	e	e	e
473	150	e	e	e
474	136	e	e	e
475	149	e	e	e
MEAN	144	--	--	--
S.D.	11.5	--	--	--
N	10	0	0	0

--: Data Unavailable e: Terminal Sacrifice

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Vehicle:Distilled Water 0 (w/w%)									
336	9.9	6.89	14.8	40.8	42	59.2	21.5	36.3	1037
337	8.4	7.70	15.0	43.3	46	56.2	19.5	34.6	988
338	5.8	7.02	14.8	41.2	42	58.7	21.1	35.9	1012
339	6.8	7.19	14.6	41.6	43	57.8	20.3	35.1	853
340	8.3	7.42	15.0	42.5	42	57.3	20.2	35.3	1087
341	5.9	7.26	14.1	39.6	43	54.6	19.4	35.6	1043
342	7.0	6.99	14.8	40.1	43	57.4	21.2	36.9	1014
343	9.0	7.05	14.7	40.6	44	57.6	20.9	36.2	1114
344	13.6	7.36	15.3	41.5	45	56.4	20.8	36.9	1243
345	4.0	7.09	14.6	39.1	42	55.1	20.6	37.3	1055
MEAN	7.9	7.20	14.8	41.0	43	57.0	20.6	36.0	1045
SD	2.66	0.244	0.32	1.28	1.4	1.47	0.70	0.87	98.9
N	10	10	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)									
356	7.4	7.08	14.5	40.4	42	57.0	20.5	35.9	1017
357	6.3	6.82	13.8	39.2	42	57.5	20.2	35.2	1044
358	4.5	6.82	14.1	39.0	42	57.2	20.7	36.2	938
359	10.0	7.33	14.9	41.6	43	56.8	20.3	35.8	1037
360	8.6	6.90	15.3	40.7	43	59.0	22.2	37.6	1035
361	8.6	7.08	14.6	40.5	43	57.2	20.6	36.0	1060
362	9.9	6.60	14.5	38.8	42	58.8	22.0	37.4	1154
363	7.6	6.98	14.8	40.1	43	57.4	21.2	36.9	1391
364	11.1	6.67	14.7	39.4	42	59.1	22.0	37.3	1085
365	11.3	7.46	15.4	42.7	46	57.3	20.6	36.1	1202
MEAN	8.5	6.97	14.7	40.2	43	57.7	21.0	36.4	1096
SD	2.15	0.273	0.49	1.23	1.2	0.88	0.76	0.80	126.6
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Mid-Low:0.55 (w/w%)									
376	8.1	7.17	14.1	39.3	42	54.8	19.7	35.9	1154
377	3.8	7.51	14.7	42.4	43	56.4	19.6	34.7	1036
378	c	c	c	c	c	c	c	c	c
379	13.3	6.99	14.8	41.3	42	59.1	21.2	35.8	1526
380	6.6	6.89	14.6	40.4	42	58.6	21.2	36.1	1044
381	5.3	6.99	15.2	41.4	44	59.2	21.7	36.7	1028
382	12.8	7.22	15.1	41.9	43	58.1	20.9	36.0	1050
383	11.8	7.59	15.9	44.2	47	58.3	20.9	36.0	912
384	8.0	7.42	15.1	41.5	44	55.9	20.4	36.4	1338
385	12.8	7.28	15.1	41.5	44	57.0	20.7	36.4	1142
MEAN	9.2	7.23	15.0	41.5	43	57.5	20.7	36.0	113
SD	3.59	0.245	0.50	1.34	1.6	1.54	0.70	0.57	187.4
N	9	9	9	9	9	9	9	9	9
GROUP: Mid:1 (w/w%)									
396	8.1	7.06	14.3	40.4	43	57.2	20.3	35.4	1074
397	14.6	7.45	15.5	44.0	46	59.0	20.8	35.2	1220
398	10.1	6.96	14.9	40.9	44	58.8	21.4	36.4	1032
399	10.1	7.61	15.7	43.8	45	57.6	20.6	35.8	1285
400	6.7	6.96	14.3	39.5	42	56.7	20.5	36.2	1022
401	11.1	6.86	14.9	41.0	43	59.7	21.7	36.3	1077
402	12.0	6.89	14.6	39.5	43	57.3	21.2	37.0	1039
403	13.0	7.23	16.1	43.1	46	59.6	22.3	37.4	998
404	12.7	6.89	14.7	40.2	43	58.4	21.3	36.6	1274
405	13.4	7.38	15.4	42.4	45	57.5	20.9	36.3	1154
MEAN	11.2	7.13	15.0	41.5	44	58.2	21.1	36.3	1118
SD	2.47	0.270	0.61	1.71	1.4	1.06	0.61	0.67	107.9
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

c - No Specimen Received

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Mid-High:3 (w/w%)									
416	a	a	a	a	a	a	a	a	a
417	a	a	a	a	a	a	a	a	a
418	a	a	a	a	a	a	a	a	a
419	a	a	a	a	a	a	a	a	a
420	a	a	a	a	a	a	a	a	a
421	a	a	a	a	a	a	a	a	a
422	a	a	a	a	a	a	a	a	a
423	10.0	7.28	15.2	41.9	45	57.5	20.9	36.3	1112
424	a	a	a	a	a	a	a	a	a
425	10.0	7.78	15.8	44.2	45	56.8	20.3	35.7	1031
MEAN	10.0	7.53	15.5	43.1	45	57.2	20.6	36.0	1072
SD	0.00	0.354	0.42	1.63	0.0	0.49	0.42	0.42	57.3
N	2	2	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)									
436	a	a	a	a	a	a	a	a	a
437	a	a	a	a	a	a	a	a	a
438	a	a	a	a	a	a	a	a	a
439	a	a	a	a	a	a	a	a	a
440	a	a	a	a	a	a	a	a	a
441	a	a	a	a	a	a	a	a	a
442	a	a	a	a	a	a	a	a	a
443	a	a	a	a	a	a	a	a	a
444	a	a	a	a	a	a	a	a	a
445	a	a	a	a	a	a	a	a	a
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0

NA - Not Applicable

a - Dead

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: (+)Control:5 (w/w%)									
456	b	b	b	b	b	b	b	b	b
457	b	b	b	b	b	b	b	b	b
458	b	b	b	b	b	b	b	b	b
459	b	b	b	b	b	b	b	b	b
460	b	b	b	b	b	b	b	b	b
461	b	b	b	b	b	b	b	b	b
462	b	b	b	b	b	b	b	b	b
463	b	b	b	b	b	b	b	b	b
464	b	b	b	b	b	b	b	b	b
465	b	b	b	b	b	b	b	b	b
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0
b - Terminal Sacrifice
NA - Not Applicable

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Vehicle:Distilled Water 0 (w/w%)									
336	6.3	434.1	0	1.4	8.3	0.2	0.0	0.0	0.0
337	3.3	254.1	0	0.8	7.6	0.0	0.0	0.0	0.0
338	4.1	287.8	0	0.9	4.8	0.1	0.1	0.0	0.0
339	4.5	323.5	0	1.0	5.7	0.1	0.1	0.0	0.0
340	5.0	371.0	0	1.2	7.1	0.1	0.0	0.0	0.0
341	3.7	268.6	0	0.9	4.8	0.0	0.1	0.0	0.0
342	5.2	363.5	0	1.1	5.4	0.3	0.2	0.0	0.0
343	4.3	303.1	0	1.3	7.7	0.1	0.0	0.0	0.0
344	3.9	287.0	0	2.2	11.2	0.3	0.0	0.0	0.0
345	3.8	269.4	0	0.7	3.3	0.0	0.0	0.0	0.0
MEAN	4.4	316.2	0.0	1.2	6.6	0.1	0.1	0.0	0.0
SD	0.88	57.09	0.00	0.43	2.26	0.11	0.07	0.00	0.00
N	10	10	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)									
356	4.9	346.9	0	0.7	6.6	0.1	0.0	0.0	0.0
357	6.7	456.9	0	1.0	4.9	0.3	0.1	0.0	0.0
358	2.8	191.0	0	0.5	4.0	0.0	0.0	0.0	0.0
359	4.3	315.2	0	1.3	8.4	0.2	0.1	0.0	0.0
360	3.5	241.5	0	1.2	7.4	0.0	0.0	0.0	0.0
361	3.4	240.7	0	1.2	7.3	0.0	0.1	0.0	0.0
362	5.7	376.2	0	1.3	8.4	0.1	0.1	0.0	0.0
363	3.8	265.2	0	1.1	6.3	0.1	0.1	0.0	0.0
364	3.4	226.8	0	1.3	9.8	0.0	0.0	0.0	0.0
365	3.0	223.8	0	1.7	9.6	0.0	0.0	0.0	0.0
MEAN	4.2	288.4	0.0	1.1	7.3	0.1	0.1	0.0	0.0
SD	1.26	83.47	0.00	0.34	1.89	0.10	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Mid-Low:0.55 (w/w%)									
376	5.2	372.8	0	1.0	7.0	0.1	0.0	0.0	0.0
377	3.6	270.4	0	0.6	3.2	0.0	0.0	0.0	0.0
378	c	c	c	c	c	c	c	c	c
379	5.1	356.5	0	1.1	12.1	0.1	0.0	0.0	0.0
380	3.5	241.1	0	1.1	5.4	0.1	0.1	0.0	0.0
381	6.3	440.4	0	1.0	4.2	0.2	0.0	0.0	0.0
382	4.7	339.3	0	1.4	11.0	0.4	0.0	0.0	0.0
383	3.3	250.5	0	1.9	9.4	0.4	0.1	0.0	0.0
384	3.4	252.3	0	1.4	6.5	0.0	0.1	0.0	0.0
385	3.4	247.5	0	2.4	10.1	0.3	0.0	0.0	0.0
MEAN	4.3	307.9	0.0	1.3	7.7	0.2	0.0	0.0	0.0
SD	1.08	71.61	0.00	0.54	3.13	0.16	0.05	0.00	0.0
N	9	9	9	9	9	9	9	9	9
GROUP: Mid:1 (w/w%)									
396	3.5	247.1	0	1.2	6.7	0.1	0.1	0.0	0.0
397	5.4	402.3	0	2.0	12.1	0.4	0.0	0.0	0.0
398	6.2	431.5	0	0.6	9.4	0.1	0.0	0.0	0.0
399	3.8	289.2	0	1.0	8.7	0.3	0.1	0.0	0.0
400	4.2	292.3	0	1.1	5.6	0.0	0.0	0.0	0.0
401	3.4	233.2	0	1.4	9.5	0.1	0.0	0.0	0.0
402	4.4	303.2	0	1.4	10.3	0.1	0.1	0.0	0.0
403	4.0	289.2	0	2.1	10.7	0.1	0.1	0.0	0.0
404	3.3	227.4	0	1.5	10.7	0.4	0.1	0.0	0.0
405	3.1	228.8	0	1.7	11.3	0.3	0.1	0.0	0.0
MEAN	4.1	294.4	0.0	1.4	9.5	0.2	0.1	0.0	0.0
SD	0.99	70.99	0.00	0.46	2.03	0.14	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

c - No Specimen Received

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Mid-High:3 (w/w%)									
416	a	a	a	a	a	a	a	a	a
417	a	a	a	a	a	a	a	a	a
418	a	a	a	a	a	a	a	a	a
419	a	a	a	a	a	a	a	a	a
420	a	a	a	a	a	a	a	a	a
421	a	a	a	a	a	a	a	a	a
422	a	a	a	a	a	a	a	a	a
423	3.0	218.4	0	1.7	8.2	0.1	0.0	0.0	0.0
424	a	a	a	a	a	a	a	a	a
425	4.9	381.2	0	1.6	8.1	0.3	0.0	0.0	0.0
MEAN	4.0	299.8	0.0	1.7	8.2	0.2	0.0	0.0	0.0
SD	1.34	115.12	0.00	0.07	0.07	0.14	0.00	0.00	0.00
N	2	2	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)									
436	a	a	a	a	a	a	a	a	a
437	a	a	a	a	a	a	a	a	a
438	a	a	a	a	a	a	a	a	a
439	a	a	a	a	a	a	a	a	a
440	a	a	a	a	a	a	a	a	a
441	a	a	a	a	a	a	a	a	a
442	a	a	a	a	a	a	a	a	a
443	a	a	a	a	a	a	a	a	a
444	a	a	a	a	a	a	a	a	a
445	a	a	a	a	a	a	a	a	a
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0
NA - Not Applicable
a - Dead

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: (+)Control:5 (w/w%)									
456	b	b	b	b	b	b	b	b	b
457	b	b	b	b	b	b	b	b	b
458	b	b	b	b	b	b	b	b	b
459	b	b	b	b	b	b	b	b	b
460	b	b	b	b	b	b	b	b	b
461	b	b	b	b	b	b	b	b	b
462	b	b	b	b	b	b	b	b	b
463	b	b	b	b	b	b	b	b	b
464	b	b	b	b	b	b	b	b	b
465	b	b	b	b	b	b	b	b	b
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0
NA - Not Applicable

b - Terminal Sacrifice

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Vehicle:Distilled Water 0 (w/w%)									
346	8.9	6.41	13.5	38.1	38	59.5	21.1	35.4	1227
347	3.9	6.41	13.5	36.6	40	57.1	21.1	36.9	1035
348	6.7	7.25	14.7	41.2	44	56.8	20.3	35.7	1170
349	6.0	6.55	14.0	38.8	42	59.3	21.4	36.1	1198
350	5.5	6.93	14.3	40.3	42	58.2	20.6	35.5	1013
351	6.5	6.64	13.3	37.5	39	56.5	20.0	35.5	1346
352	6.5	6.67	13.9	38.2	41	57.3	20.8	36.4	1179
353	5.5	6.50	14.3	39.2	43	60.3	22.0	36.5	1245
354	6.6	6.34	13.5	37.1	40	58.5	21.3	36.4	1059
355	6.5	6.63	13.7	37.7	40	56.8	20.7	36.3	1102
MEAN	6.3	6.63	13.9	38.5	41	58.0	20.9	36.1	1157
SD	1.26	0.275	0.45	1.44	1.9	1.33	0.58	0.51	104.9
N	10	10	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)									
366	4.6	5.99	13.0	36.2	38	60.5	21.7	35.9	1163
367	4.6	6.85	13.6	37.4	39	54.6	19.9	36.4	948
368	3.3	6.80	14.3	39.8	41	58.5	21.0	35.9	1067
369	7.4	6.89	14.2	39.3	40	57.0	20.6	36.1	1238
370	8.3	6.98	14.5	40.0	43	57.3	20.8	36.3	1126
371	5.2	6.60	14.5	39.3	42	59.5	22.0	36.9	1134
372	7.1	6.70	14.1	39.1	41	58.3	21.0	36.1	1157
373	5.8	6.72	13.7	37.9	40	56.4	20.4	36.1	1166
374	7.0	7.34	14.6	41.2	43	56.1	19.9	35.4	1103
375	8.7	7.40	14.5	40.3	42	54.5	19.6	36.0	1202
MEAN	6.2	6.83	14.1	39.1	41	57.3	20.7	36.1	1130
SD	1.77	0.394	0.52	1.49	1.7	1.97	0.78	0.39	80.1
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Mid-Low:0.55 (w/w%)									
386	3.0	6.82	14.0	39.6	40	58.0	20.5	35.4	1075
387	4.1	6.76	14.0	38.9	42	57.5	20.7	36.0	1078
388	2.0	5.43	11.6	33.0	34	60.8	21.4	35.2	1856
389	6.2	6.78	14.9	41.5	43	61.2	22.0	35.9	1309
390	6.3	6.48	13.7	38.1	40	58.8	21.1	36.0	1125
391	7.6	7.50	14.9	42.3	44	56.4	19.9	35.2	1022
392	12.0	6.73	14.0	38.6	41	57.3	20.8	36.3	1148
393	16.1	7.69	15.7	43.8	45	57.0	20.4	35.8	1058
394	5.7	6.54	14.0	38.3	40	58.6	21.4	36.6	908
395	7.2	6.70	14.5	41.2	44	61.5	21.6	35.2	1142
MEAN	7.0	6.74	14.1	39.5	41	58.7	21.0	35.8	1172
SD	4.22	0.607	1.08	2.98	3.2	1.84	0.64	0.49	261.1
N	10	10	10	10	10	10	10	10	10
GROUP: Mid:1 (w/w%)									
406	8.7	6.67	14.8	40.9	43	61.3	22.2	36.2	1101
407	4.8	7.26	15.2	43.2	45	59.5	20.9	35.2	1017
408	6.0	6.48	13.7	38.4	40	59.2	21.1	35.7	1046
409	5.5	7.53	15.0	42.8	44	56.8	19.9	35.0	1130
410	4.0	6.90	13.8	39.9	40	57.8	20.0	34.6	1088
411	6.2	6.99	14.0	39.9	40	57.1	20.0	35.1	1144
412	5.5	6.35	13.5	37.9	38	59.7	21.3	35.6	1117
413	8.1	7.28	14.7	41.4	43	56.8	20.2	35.5	1163
414	9.1	6.95	14.2	39.9	43	57.4	20.4	35.6	1112
415	8.3	6.61	13.6	37.7	40	57.1	20.6	36.1	1172
MEAN	6.6	6.90	14.3	40.2	42	58.3	20.7	35.5	1109
SD	1.79	0.380	0.63	1.91	2.3	1.55	0.73	0.49	48.9
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Mid-High:3 (w/w%)									
426	5.4	6.92	14.7	40.5	43	58.5	21.2	36.3	1127
427	a	a	a	a	a	a	a	a	a
428	a	a	a	a	a	a	a	a	a
429	a	a	a	a	a	a	a	a	a
430	a	a	a	a	a	a	a	a	a
431	a	a	a	a	a	a	a	a	a
432	6.7	7.05	14.6	40.3	42	57.2	20.7	36.2	1080
433	a	a	a	a	a	a	a	a	a
434	a	a	a	a	a	a	a	a	a
435	a	a	a	a	a	a	a	a	a
MEAN	6.1	6.99	14.7	40.4	43	57.8	21.0	36.3	1104
SD	0.92	0.092	0.07	0.14	0.7	0.92	0.35	0.07	33.2
N	2	2	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)									
446	a	a	a	a	a	a	a	a	a
447	a	a	a	a	a	a	a	a	a
448	a	a	a	a	a	a	a	a	a
449	a	a	a	a	a	a	a	a	a
450	a	a	a	a	a	a	a	a	a
451	a	a	a	a	a	a	a	a	a
452	a	a	a	a	a	a	a	a	a
453	a	a	a	a	a	a	a	a	a
454	a	a	a	a	a	a	a	a	a
455	a	a	a	a	a	a	a	a	a
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0

a - Dead

NA - Not Applicable

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: (+)Control:5 (w/w%)									
466	b	b	b	b	b	b	b	b	b
467	b	b	b	b	b	b	b	b	b
468	b	b	b	b	b	b	b	b	b
469	b	b	b	b	b	b	b	b	b
470	b	b	b	b	b	b	b	b	b
471	b	b	b	b	b	b	b	b	b
472	b	b	b	b	b	b	b	b	b
473	b	b	b	b	b	b	b	b	b
474	b	b	b	b	b	b	b	b	b
475	b	b	b	b	b	b	b	b	b
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0
NA - Not Applicable
b - Terminal Sacrifice

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Vehicle:Distilled Water 0 (w/w%)									
346	3.4	217.9	0	1.6	7.2	0.1	0.0	0.0	0.0
347	4.5	288.5	0	0.5	3.3	0.0	0.0	0.0	0.0
348	2.7	195.8	0	0.5	6.1	0.1	0.0	0.0	0.0
349	3.2	209.6	0	0.7	5.2	0.0	0.1	0.0	0.0
350	3.6	249.5	0	0.9	4.6	0.0	0.1	0.0	0.0
351	3.8	252.3	0	0.1	6.0	0.3	0.1	0.0	0.0
352	4.3	286.8	0	0.7	5.7	0.1	0.0	0.0	0.0
353	5.1	331.5	0	1.0	4.5	0.1	0.0	0.0	0.0
354	3.1	196.5	0	1.0	5.5	0.1	0.0	0.0	0.0
355	3.1	205.5	0	0.3	6.0	0.0	0.1	0.0	0.0
MEAN	3.7	243.4	0.0	0.7	5.4	0.1	0.0	0.0	0.0
SD	0.75	46.54	0.00	0.42	1.08	0.09	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)									
366	5.5	329.5	0	0.7	3.9	0.0	0.0	0.0	0.0
367	3.6	246.6	0	0.6	4.0	0.0	0.0	0.0	0.0
368	5.0	340.0	0	0.4	2.8	0.1	0.0	0.0	0.0
369	3.9	268.7	0	0.8	6.6	0.0	0.0	0.0	0.0
370	3.5	244.3	0	1.2	7.1	0.0	0.0	0.0	0.0
371	3.3	217.8	0	0.6	4.4	0.1	0.1	0.0	0.0
372	3.9	261.3	0	0.8	6.2	0.1	0.0	0.0	0.0
373	3.4	228.5	0	0.7	5.0	0.1	0.0	0.0	0.0
374	3.6	264.2	0	0.7	6.1	0.1	0.1	0.0	0.0
375	2.9	214.6	0	0.7	7.7	0.2	0.1	0.0	0.0
MEAN	3.9	261.5	0.0	0.7	5.4	0.1	0.0	0.0	0.0
SD	0.80	42.90	0.00	0.20	1.59	0.07	0.05	0.00	0.00
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Mid-Low:0.55 (w/w%)									
386	4.3	293.3	0	0.3	2.6	0.0	0.0	0.0	0.0
387	4.4	297.4	0	0.7	3.4	0.0	0.0	0.0	0.0
388	6.9	374.7	0	0.2	1.7	0.1	0.0	0.0	0.0
389	4.8	325.4	0	0.5	5.5	0.1	0.2	0.0	0.0
390	4.1	265.7	0	0.6	5.6	0.1	0.0	0.0	0.0
391	2.8	210.0	0	1.3	6.1	0.2	0.1	0.0	0.0
392	3.0	201.9	0	1.3	10.7	0.0	0.0	0.0	0.0
393	2.9	223.0	0	1.6	14.2	0.2	0.2	0.0	0.0
394	2.9	189.7	0	0.8	4.8	0.1	0.0	0.0	0.0
395	2.9	194.3	0	1.0	6.0	0.1	0.0	0.0	0.0
MEAN	3.9	257.5	0.0	0.8	6.1	0.1	0.1	0.0	0.0
SD	1.30	63.61	0.00	0.46	3.77	0.07	0.08	0.00	0.00
N	10	10	10	10	10	10	10	10	10
GROUP: Mid:1 (w/w%)									
406	2.8	186.8	0	1.4	7.2	0.1	0.0	0.0	0.0
407	3.4	246.8	0	0.5	4.3	0.0	0.0	0.0	0.0
408	3.8	246.2	0	0.9	4.9	0.1	0.1	0.0	0.0
409	3.3	248.5	0	0.7	4.7	0.1	0.1	0.0	0.0
410	2.9	200.1	0	0.6	3.2	0.2	0.0	0.0	0.0
411	2.9	202.7	0	0.7	5.3	0.2	0.0	0.0	0.0
412	4.7	298.5	0	0.7	4.8	0.0	0.0	0.0	0.0
413	3.2	233.0	0	1.0	7.0	0.0	0.1	0.0	0.0
414	3.6	250.2	0	1.5	7.5	0.2	0.0	0.0	0.0
415	3.2	211.5	0	0.8	7.1	0.2	0.2	0.0	0.0
MEAN	3.4	232.4	0.0	0.9	5.6	0.1	0.1	0.0	0.0
SD	0.56	32.97	0.00	0.33	1.49	0.09	0.07	0.00	0.00
N	10	10	10	10	10	10	10	10	10

WBC corrected for NRBC > 0

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Mid-High:3 (w/w%)									
426	3.3	228.4	0	0.7	4.7	0.0	0.0	0.0	0.0
427	a	a	a	a	a	a	a	a	a
428	a	a	a	a	a	a	a	a	a
429	a	a	a	a	a	a	a	a	a
430	a	a	a	a	a	a	a	a	a
431	a	a	a	a	a	a	a	a	a
432	2.8	197.4	0	0.9	5.6	0.1	0.1	0.0	0.0
433	a	a	a	a	a	a	a	a	a
434	a	a	a	a	a	a	a	a	a
435	a	a	a	a	a	a	a	a	a
MEAN	3.1	212.9	0.0	0.8	5.2	0.1	0.1	0.0	0.0
SD	0.35	21.92	0.00	0.14	0.64	0.07	0.07	0.00	0.00
N	2	2	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)									
446	a	a	a	a	a	a	a	a	a
447	a	a	a	a	a	a	a	a	a
448	a	a	a	a	a	a	a	a	a
449	a	a	a	a	a	a	a	a	a
450	a	a	a	a	a	a	a	a	a
451	a	a	a	a	a	a	a	a	a
452	a	a	a	a	a	a	a	a	a
453	a	a	a	a	a	a	a	a	a
454	a	a	a	a	a	a	a	a	a
455	a	a	a	a	a	a	a	a	a
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0

a - Dead

NA - Not Applicable

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: Terminal

STUDY ID: 1052SN3

SEX: FEMALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: (+)Control:5 (w/w%)									
466	b	b	b	b	b	b	b	b	b
467	b	b	b	b	b	b	b	b	b
468	b	b	b	b	b	b	b	b	b
469	b	b	b	b	b	b	b	b	b
470	b	b	b	b	b	b	b	b	b
471	b	b	b	b	b	b	b	b	b
472	b	b	b	b	b	b	b	b	b
473	b	b	b	b	b	b	b	b	b
474	b	b	b	b	b	b	b	b	b
475	b	b	b	b	b	b	b	b	b
MEAN	NA	NA	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0	0	0

WBC corrected for NRBC > 0
NA - Not Applicable

b - Terminal Sacrifice

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: MALE

GROUP: Vehicle : Distilled Water 0 (w/w%)

Animal ID	Terminal
336	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
337	Polychromasia +; Platelets Adequate and Normal
338	Polychromasia +; Anisocytosis +; Poikilocytosis +; Platelets Adequate and Normal
339	Polychromasia +; Platelets Adequate and Normal
340	Polychromasia +; Platelets Adequate and Normal
341	Polychromasia +; Platelets Adequate and Normal
342	Polychromasia +; Poikilocytosis +; Platelets Adequate and Normal
343	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: MALE

GROUP: Vehicle : Distilled Water 0 (w/w%)

Animal ID	Terminal
344	Polychromasia +; Platelets Adequate and Normal
345	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: MALE

GROUP: Low : 0.25 (w/w%)

Animal ID	Terminal
356	Polychromasia +; Platelets Adequate and Normal
357	Polychromasia +; Anisocytosis +; Target Cells +; Platelets Adequate and Normal
358	Polychromasia +; Platelets Adequate and Normal
359	Polychromasia +; Platelets Adequate and Normal
360	Polychromasia +; Platelets Adequate and Normal
361	Polychromasia +; Poikilocytosis +; Platelets Adequate and Normal
362	Polychromasia +; Platelets Adequate and Normal
363	Polychromasia +; Anisocytosis +; Platelets Increased and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: MALE

GROUP: Low : 0.25 (w/w%)

Animal ID	Terminal
364	Polychromasia +; Platelets Adequate and Normal
365	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: MALE

GROUP: Mid-Low : 0.55 (w/w%)

Animal ID	Terminal
376	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
377	Polychromasia +; Platelets Adequate and Normal
378	c
379	Polychromasia +; Platelets Adequate and Normal
380	Polychromasia +; Platelets Adequate and Normal
381	Polychromasia +; Target Cells +; Platelets Adequate and Normal
382	Polychromasia +; Platelets Adequate and Normal
383	Polychromasia +; Platelets Adequate and Normal
384	Polychromasia +; Anisocytosis +; Platelets Incressed and Normal

c - No Specimen Received

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: MALE

GROUP: Mid-Low : 0.55 (w/w%)

Animal ID	Terminal
385	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: MALE

GROUP: Mid : 1 (w/w%)

Animal ID	Terminal
396	Polychromasia +; Platelets Adequate and Normal
397	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
398	Polychromasia +; Platelets Adequate and Normal
399	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
400	Polychromasia +; Platelets Adequate and Normal
401	Polychromasia +; Platelets Adequate and Normal
402	Polychromasia +; Platelets Adequate and Normal
403	Polychromasia +; Platelets Adequate and Normal
404	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: MALE

GROUP: Mid : 1 (w/w%)

Animal ID	Terminal
405	Polychromasia +; Platelets Adequate and Normal

Appendix H

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: MALE

GROUP: Mid-High : 3 (w/w%)

Animal ID	Terminal
416	a
417	a
418	a
419	a
420	a
421	a
422	a
423	Polychromasia +; Platelets Adequate and Normal
424	a
425	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal

a - Dead

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: MALE

GROUP: High : 5 (w/w%)

Animal ID	Terminal
436	a
437	a
438	a
439	a
440	a
441	a
442	a
443	a
444	a
445	a

a - Dead

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: MALE

GROUP: (+)Control : 5 (w/w%)

Animal ID	Terminal
456	b
457	b
458	b
459	b
460	b
461	b
462	b
463	b
464	b
465	b

b - Terminal Sacrifice

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: FEMALE

GROUP: Vehicle : Distilled Water 0 (w/w%)

Animal ID	Terminal
346	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
347	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
348	Polychromasia +; Platelets Adequate and Normal
349	Polychromasia +; Platelets Adequate and Normal
350	Polychromasia +; Platelets Adequate and Normal
351	Polychromasia ++; Anisocytosis +; Platelets Increased and Normal
352	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
353	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: FEMALE

GROUP: Vehicle : Distilled Water 0 (w/w%)

Animal ID	Terminal
354	Polychromasia +; Platelets Adequate and Normal
355	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: FEMALE

GROUP: Low : 0.25 (w/w%)

Animal ID	Terminal
366	Polychromasia +; Anisocytosis +; Target Cells +; Platelets Adequate and Normal
367	Polychromasia +; Platelets Adequate and Normal
368	Polychromasia +; Platelets Adequate and Normal
369	Polychromasia +; Platelets Adequate and Normal
370	Polychromasia +; Platelets Adequate and Normal
371	Polychromasia +; Platelets Adequate and Normal
372	Polychromasia ++; Anisocytosis +; Poikilocytosis +; Platelets Adequate and Normal
373	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: FEMALE

GROUP: Low : 0.25 (w/w%)

Animal ID	Terminal
374	Polychromasia +; Platelets Adequate and Normal
375	Polychromasia +; Anisocytosis +; Poikilocytosis +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: FEMALE

GROUP: Mid-Low : 0.55 (w/w%)

Animal ID	Terminal
386	Polychromasia +; Platelets Adequate and Normal
387	Polychromasia +; Platelets Adequate and Normal
388	Polychromasia +++; Anisocytosis ++; Poikilocytosis +; Platelets Increased and Normal
389	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Increased and Normal
390	Polychromasia +; Platelets Adequate and Normal
391	Polychromasia +; Platelets Adequate and Normal
392	Polychromasia +; Platelets Adequate and Normal
393	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: FEMALE

GROUP: Mid-Low : 0.55 (w/w%)

Animal ID	Terminal
394	Polychromasia +; Platelets Adequate and Normal
395	Polychromasia +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: FEMALE

GROUP: Mid : 1 (w/w%)

Animal ID	Terminal
406	Polychromasia +; Platelets Adequate and Normal
407	Polychromasia +; Platelets Adequate and Normal
408	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
409	Polychromasia +; Platelets Adequate and Normal
410	Polychromasia +; Platelets Adequate and Normal
411	Polychromasia +; Platelets Adequate and Normal
412	Polychromasia +; Platelets Adequate and Normal
413	Polychromasia +; Platelets Adequate and Normal
414	Polychromasia +; Platelets Adequate and Normal

Appendix H

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: FEMALE

GROUP: Mid : 1 (w/w%)

Animal ID	Terminal
415	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3

SEX: FEMALE

GROUP: Mid-High : 3 (w/w%)

Animal ID	Terminal
426	Polychromasia +; Platelets Adequate and Normal
427	a
428	a
429	a
430	a
431	a
432	Polychromasia +; Platelets Adequate and Normal
433	a
434	a
435	a

a - Dead

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: FEMALE

GROUP: High : 5 (w/w%)

Animal ID	Terminal
446	a
447	a
448	a
449	a
450	a
451	a
452	a
453	a
454	a
455	a

a - Dead

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052SN3 SEX: FEMALE

GROUP: (+)Control : 5 (w/w%)

Animal ID	Terminal
466	b
467	b
468	b
469	b
470	b
471	b
472	b
473	b
474	b
475	b

b - Terminal Sacrifice

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: Vehicle:Distilled Water 0 (w/w%)							
336	145	4.4	105	9.1	7.8	26	24
337	145	4.4	105	9.5	8.1	24	--
338	143	4.0	106	9.5	7.2	20	--
339	144	4.0	105	9.7	7.6	28	13
340	146	3.9	105	10.0	7.9	21	19
341	144	4.3	105	9.9	8.3	18	11
342	146	4.1	107	9.9	7.8	21	14
343	146	4.1	106	9.5	8.6	18	--
344	143	4.7	104	9.9	8.9	30	26
345	141	5.4	112	9.6	8.4	25	15
MEAN	144	4.3	106	9.7	8.1	23	17
SD	1.6	0.45	2.3	0.28	0.50	4.1	5.7
N	10	10	10	10	10	10	7
GROUP: Low:0.25 (w/w%)							
356	145	4.1	106	9.3	7.4	23	--
357	143	4.3	106	9.4	8.0	23	--
358	144	3.7	106	9.3	7.8	28	20
359	143	4.2	105	9.8	7.7	24	13
360	144	4.0	104	9.6	8.5	21	11
361	143	4.1	104	9.6	8.1	26	11
362	145	4.2	105	9.5	8.2	21	12
363	146	4.7	105	9.2	8.3	25	12
364	142	4.5	103	10.1	7.4	28	23
365	143	4.5	105	9.7	8.7	22	18
MEAN	144	4.2	105	9.6	8.0	24	15
SD	1.2	0.29	1.0	0.27	0.44	2.6	4.7
N	10	10	10	10	10	10	8

(--) - Data Unavailable
(--) - Data Unavailable = Below Detection Limit For TG

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: Mid-Low:0.55 (w/w%)							
376	143	4.3	104	9.6	7.7	23	--
377	143	4.2	105	9.4	7.9	24	--
378	--	--	--	--	--	--	--
379	143	4.6	105	9.8	8.0	31	13
380	143	4.2	105	9.5	7.7	23	12
381	144	4.2	105	9.9	8.6	25	17
382	145	4.0	105	9.3	7.1	18	13
383	143	4.4	105	9.8	7.8	28	21
384	144	4.2	106	9.7	8.5	25	12
385	145	4.3	107	9.6	8.5	21	--
MEAN	144	4.3	105	9.6	8.0	24	15
SD	0.9	0.17	0.8	0.20	0.49	3.8	3.6
N	9	9	9	9	9	9	6
GROUP: Mid:1 (w/w%)							
396	145	4.1	107	9.1	6.8	26	--
397	142	4.8	104	9.9	8.2	23	--
398	143	4.3	106	9.8	8.3	25	19
399	144	4.5	106	9.7	8.0	28	--
400	145	4.2	105	9.4	7.1	20	10
401	144	4.2	106	9.9	7.5	28	10
402	142	4.4	105	9.6	8.7	28	12
403	147	3.9	105	9.9	7.8	26	--
404	143	4.4	107	10.1	7.9	25	27
405	144	4.5	106	10.0	8.5	25	16
MEAN	144	4.3	106	9.7	7.9	25	16
SD	1.5	0.25	0.9	0.30	0.60	2.5	6.6
N	10	10	10	10	10	10	6

(--) - Data Unavailable
(--) - Data Unavailable = Below Detection Limit For TG

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: Mid-High:3 (w/w%)							
416	x	x	x	x	x	x	x
417	x	x	x	x	x	x	x
418	x	x	x	x	x	x	x
419	x	x	x	x	x	x	x
420	x	x	x	x	x	x	x
421	x	x	x	x	x	x	x
422	x	x	x	x	x	x	x
423	143	4.3	105	10.0	8.2	41	17
424	x	x	x	x	x	x	x
425	145	4.3	106	10.0	8.6	29	21
MEAN	144	4.3	106	10.0	8.4	35	19
SD	1.4	0.00	0.7	0.00	0.28	8.5	2.8
N	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)							
436	x	x	x	x	x	x	x
437	x	x	x	x	x	x	x
438	x	x	x	x	x	x	x
439	x	x	x	x	x	x	x
440	x	x	x	x	x	x	x
441	x	x	x	x	x	x	x
442	x	x	x	x	x	x	x
443	x	x	x	x	x	x	x
444	x	x	x	x	x	x	x
445	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: (+)Control:5 (w/w%)							
456	x	x	x	x	x	x	x
457	x	x	x	x	x	x	x
458	x	x	x	x	x	x	x
459	x	x	x	x	x	x	x
460	x	x	x	x	x	x	x
461	x	x	x	x	x	x	x
462	x	x	x	x	x	x	x
463	x	x	x	x	x	x	x
464	x	x	x	x	x	x	x
465	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: Vehicle:Distilled Water 0 (w/w%)							
336	1032	121	30	130	0.49	12.6	23.7
337	1091	177	30	138	0.54	12.0	19.3
338	1147	166	32	158	0.45	8.0	17.8
339	827	159	33	114	0.59	7.4	47.6
340	177	203	24	63	0.59	13.6	31.1
341	839	118	27	105	0.53	11.6	54.5
342	690	130	31	110	0.46	14.6	16.7
343	1227	174	38	162	0.45	22.4	54.8
344	1715	300	31	176	0.42	14.0	137.9
345	221	189	24	77	0.40	9.6	35.1
MEAN	897	174	30	123	0.49	12.6	43.8
SD	462.2	52.8	4.2	36.7	0.068	4.24	36.14
N	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)							
356	1095	151	27	117	0.43	15.0	59.7
357	720	274	34	110	0.54	10.0	36.5
358	1267	140	27	139	0.61	7.4	21.8
359	444	217	30	95	0.46	15.8	67.7
360	1698	217	32	177	0.49	12.0	23.9
361	852	177	30	127	0.51	12.4	71.3
362	1883	170	31	155	0.48	10.4	44.2
363	1707	131	37	167	0.41	8.8	19.1
364	889	97	33	111	0.48	16.0	21.9
365	1768	169	31	166	0.36	10.0	37.7
MEAN	1232	174	31	136	0.48	11.8	40.4
SD	507.6	50.8	3.0	28.5	0.070	3.00	19.79
N	10	10	10	10	10	10	10

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: Mid-Low:0.55 (w/w%)							
376	865	163	34	119	0.52	10.6	193.3
377	1503	144	32	123	0.31	11.2	34.8
378	--	--	--	--	--	--	--
379	1075	100	32	126	0.46	12.2	39.0
380	1435	178	31	137	0.60	8.4	46.7
381	1284	234	31	147	0.69	14.8	42.2
382	1179	179	32	183	0.55	12.4	20.1
383	1226	163	27	126	0.68	9.2	26.6
384	1193	156	26	136	0.45	11.2	22.9
385	868	142	29	133	0.48	9.0	41.1
MEAN	1181	162	30	137	0.53	11.0	51.9
SD	220.8	35.9	2.6	19.3	0.120	2.00	53.83
N	9	9	9	9	9	9	9
GROUP: Mid:1 (w/w%)							
396	963	148	30	124	0.57	10.4	54.5
397	365	209	35	114	0.49	26.2	92.6
398	1836	153	30	174	0.54	8.6	70.3
399	818	166	31	114	0.46	16.4	17.6
400	1171	154	27	135	0.52	10.4	31.0
401	1007	199	27	124	0.54	10.4	41.9
402	2052	166	30	193	0.47	10.2	145.8
403	800	155	24	123	0.49	14.4	59.5
404	325	150	30	90	0.62	14.4	30.2
405	1259	144	36	160	0.56	15.0	24.9
MEAN	1060	164	30	135	0.53	13.6	56.8
SD	557.8	22.1	3.6	31.3	0.050	5.13	38.80
N	10	10	10	10	10	10	10

(--) - Data Unavailable

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INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: Mid-High:3 (w/w%)							
416	x	x	x	x	x	x	x
417	x	x	x	x	x	x	x
418	x	x	x	x	x	x	x
419	x	x	x	x	x	x	x
420	x	x	x	x	x	x	x
421	x	x	x	x	x	x	x
422	x	x	x	x	x	x	x
423	564	194	24	100	0.48	9.4	19.2
424	x	x	x	x	x	x	x
425	179	168	26	70	0.47	8.6	29.1
MEAN	372	181	25	85	0.48	9.0	24.2
SD	272.2	18.4	1.4	21.2	0.007	0.57	7.00
N	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)							
436	x	x	x	x	x	x	x
437	x	x	x	x	x	x	x
438	x	x	x	x	x	x	x
439	x	x	x	x	x	x	x
440	x	x	x	x	x	x	x
441	x	x	x	x	x	x	x
442	x	x	x	x	x	x	x
443	x	x	x	x	x	x	x
444	x	x	x	x	x	x	x
445	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

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INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: (+)Control:5 (w/w%)							
456	x	x	x	x	x	x	x
457	x	x	x	x	x	x	x
458	x	x	x	x	x	x	x
459	x	x	x	x	x	x	x
460	x	x	x	x	x	x	x
461	x	x	x	x	x	x	x
462	x	x	x	x	x	x	x
463	x	x	x	x	x	x	x
464	x	x	x	x	x	x	x
465	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: Vehicle:Distilled Water 0 (w/w%)							
336	13	0.5	131	5.0	3.3	1.7	1.9
337	14	0.6	118	5.4	3.7	1.7	2.2
338	14	0.5	111	5.3	3.6	1.7	2.1
339	14	0.4	87	5.1	3.7	1.4	2.6
340	15	0.5	125	5.4	3.7	1.7	2.2
341	16	0.4	106	5.2	3.4	1.8	1.9
342	14	0.4	115	5.2	3.6	1.6	2.3
343	18	0.4	78	5.2	3.6	1.6	2.3
344	16	0.5	88	5.4	3.7	1.7	2.2
345	19	0.5	75	4.6	3.2	1.4	2.3
MEAN	15	0.5	103	5.2	3.6	1.6	2.2
SD	1.9	0.07	20.0	0.24	0.18	0.13	0.21
N	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)							
356	14	0.6	107	5.2	3.6	1.6	2.3
357	13	0.3	103	4.9	3.3	1.6	2.1
358	13	0.3	97	5.0	3.6	1.4	2.6
359	14	0.5	140	5.3	3.8	1.5	2.5
360	17	0.4	96	5.0	3.5	1.5	2.3
361	15	0.4	109	5.0	3.5	1.5	2.3
362	15	0.5	93	4.9	3.6	1.3	2.8
363	14	0.3	107	5.1	3.3	1.8	1.8
364	12	0.4	108	5.2	3.5	1.7	2.1
365	14	0.4	100	5.3	3.5	1.8	1.9
MEAN	14	0.4	106	5.1	3.5	1.6	2.3
SD	1.4	0.10	13.2	0.15	0.15	0.16	0.31
N	10	10	10	10	10	10	10

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INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: Mid-Low:0.55 (w/w%)							
376	18	0.5	110	5.4	3.7	1.7	2.2
377	20	0.5	137	5.1	3.5	1.6	2.2
378	--	--	--	--	--	--	--
379	18	0.5	102	5.2	3.1	2.1	1.5
380	14	0.5	83	5.2	3.5	1.7	2.1
381	13	0.4	88	5.2	3.7	1.5	2.5
382	13	0.5	87	5.1	3.5	1.6	2.2
383	16	0.4	115	5.3	3.5	1.8	1.9
384	13	0.4	93	5.3	3.6	1.7	2.1
385	16	0.4	100	5.2	3.4	1.8	1.9
MEAN	16	0.5	102	5.2	3.5	1.7	2.1
SD	2.6	0.05	17.0	0.10	0.18	0.17	0.28
N	9	9	9	9	9	9	9
GROUP: Mid:1 (w/w%)							
396	19	0.6	99	5.1	3.5	1.6	2.2
397	17	0.5	141	5.5	3.9	1.6	2.4
398	20	0.4	112	5.5	3.8	1.7	2.2
399	16	0.5	102	5.3	3.6	1.7	2.1
400	14	0.5	110	5.0	3.5	1.5	2.3
401	14	0.4	92	5.3	3.8	1.5	2.5
402	16	0.4	88	5.0	3.4	1.6	2.1
403	14	0.3	108	5.3	3.6	1.7	2.1
404	16	0.5	112	5.5	3.6	1.9	1.9
405	17	0.5	106	5.6	3.7	1.9	1.9
MEAN	16	0.5	107	5.3	3.6	1.7	2.2
SD	2.1	0.08	14.5	0.22	0.16	0.14	0.19
N	10	10	10	10	10	10	10

(--) - Data Unavailable

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: Mid-High:3 (w/w%)							
416	x	x	x	x	x	x	x
417	x	x	x	x	x	x	x
418	x	x	x	x	x	x	x
419	x	x	x	x	x	x	x
420	x	x	x	x	x	x	x
421	x	x	x	x	x	x	x
422	x	x	x	x	x	x	x
423	14	0.4	89	5.1	3.4	1.7	2.0
424	x	x	x	x	x	x	x
425	12	0.4	102	5.2	3.4	1.8	1.9
MEAN	13	0.4	96	5.2	3.4	1.8	2.0
SD	1.4	0.00	9.2	0.07	0.00	0.07	0.07
N	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)							
436	x	x	x	x	x	x	x
437	x	x	x	x	x	x	x
438	x	x	x	x	x	x	x
439	x	x	x	x	x	x	x
440	x	x	x	x	x	x	x
441	x	x	x	x	x	x	x
442	x	x	x	x	x	x	x
443	x	x	x	x	x	x	x
444	x	x	x	x	x	x	x
445	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: MALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: (+)Control:5 (w/wX)							
456	x	x	x	x	x	x	x
457	x	x	x	x	x	x	x
458	x	x	x	x	x	x	x
459	x	x	x	x	x	x	x
460	x	x	x	x	x	x	x
461	x	x	x	x	x	x	x
462	x	x	x	x	x	x	x
463	x	x	x	x	x	x	x
464	x	x	x	x	x	x	x
465	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: Vehicle:Distilled Water 0 (w/w%)							
346	142	3.8	104	9.5	6.4	32	17
347	143	3.7	107	9.4	7.7	43	--
348	146	4.0	105	10.0	6.5	36	15
349	141	3.8	106	9.4	6.0	30	10
350	141	3.7	106	9.8	6.1	28	14
351	144	4.2	107	9.8	6.5	29	--
352	144	3.8	103	9.4	7.2	41	17
353	143	3.7	105	9.6	7.8	15	--
354	145	4.0	105	9.5	8.6	30	23
355	143	4.0	108	9.4	7.0	28	10
MEAN	143	3.9	106	9.6	7.0	31	15
SD	1.6	0.17	1.5	0.21	0.84	7.8	4.5
N	10	10	10	10	10	10	7
GROUP: Low:0.25 (w/w%)							
366	143	3.8	105	9.8	5.5	31	13
367	142	3.5	105	9.4	5.9	26	15
368	143	3.9	105	9.7	5.8	42	12
369	142	4.0	106	9.8	7.4	29	10
370	142	3.4	102	9.3	7.3	33	20
371	143	4.1	109	9.5	8.0	23	--
372	145	4.0	107	9.3	7.2	23	15
373	145	4.0	107	9.6	7.6	20	10
374	143	3.5	105	9.6	8.2	30	14
375	143	3.8	107	9.6	7.9	32	11
MEAN	143	3.8	106	9.6	7.1	29	13
SD	1.1	0.25	1.9	0.18	0.99	6.3	3.2
N	10	10	10	10	10	10	9

(--) - Data Unavailable
(--) - Data Unavailable = Below Detection Limit for TG

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: Mid-Low:0.55 (w/w%)							
386	143	3.7	107	9.4	6.2	26	11
387	141	3.7	108	9.2	4.9	23	--
388	141	6.3	110	9.3	8.2	23	17
389	143	3.9	103	9.6	6.7	36	11
390	142	4.0	105	9.5	7.2	33	15
391	142	3.9	106	9.6	6.3	22	12
392	143	4.2	108	9.7	8.3	27	12
393	143	3.8	106	10.0	8.5	23	--
394	144	3.9	108	9.5	7.4	19	--
395	142	3.9	107	10.1	8.2	28	12
MEAN	142	4.1	107	9.6	7.2	26	13
SD	1.0	0.78	1.9	0.28	1.17	5.2	2.3
N	10	10	10	10	10	10	7
GROUP: Mid:1 (w/w%)							
406	143	3.6	106	9.5	6.4	30	--
407	143	3.9	107	9.7	6.4	32	14
408	144	3.8	110	9.4	7.2	19	10
409	142	3.9	105	9.6	6.9	30	16
410	143	3.9	106	10.0	6.8	24	--
411	142	3.9	108	9.7	6.9	38	13
412	143	4.0	106	9.7	8.0	36	14
413	143	4.3	107	9.8	7.9	35	13
414	142	4.1	106	10.0	7.6	22	--
415	141	3.6	105	9.5	7.0	24	11
MEAN	143	3.9	107	9.7	7.1	29	13
SD	0.8	0.21	1.5	0.20	0.56	6.5	2.0
N	10	10	10	10	10	10	7

(--) - Data Unavailable
(--) - Data Unavailable = Below Detection Limit For TG

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3

SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: Mid-High:3 (w/w%)							
426	145	4.0	106	9.5	6.9	27	16
427	x	x	x	x	x	x	x
428	x	x	x	x	x	x	x
429	x	x	x	x	x	x	x
430	x	x	x	x	x	x	x
431	x	x	x	x	x	x	x
432	145	3.5	105	9.6	7.2	33	18
433	x	x	x	x	x	x	x
434	x	x	x	x	x	x	x
435	x	x	x	x	x	x	x
MEAN	145	3.8	106	9.6	7.1	30	17
SD	0.0	0.35	0.7	0.07	0.21	4.2	1.4
N	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)							
446	x	x	x	x	x	x	x
447	x	x	x	x	x	x	x
448	x	x	x	x	x	x	x
449	x	x	x	x	x	x	x
450	x	x	x	x	x	x	x
451	x	x	x	x	x	x	x
452	x	x	x	x	x	x	x
453	x	x	x	x	x	x	x
454	x	x	x	x	x	x	x
455	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CL mmol/L	CA mg/dL	PO4 mg/dL	CHOL mg/dL	TG mg/dL
GROUP: (+)Control:5 (w/w%)							
466	x	x	x	x	x	x	x
467	x	x	x	x	x	x	x
468	x	x	x	x	x	x	x
469	x	x	x	x	x	x	x
470	x	x	x	x	x	x	x
471	x	x	x	x	x	x	x
472	x	x	x	x	x	x	x
473	x	x	x	x	x	x	x
474	x	x	x	x	x	x	x
475	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: Vehicle:Distilled Water 0 (w/w%)							
346	1543	135	35	171	0.49	15.5	25.7
347	996	79	32	142	0.54	9.7	32.7
348	720	73	30	110	0.51	14.1	29.0
349	1423	152	50	163	0.51	10.6	25.2
350	178	79	26	77	0.46	11.3	20.9
351	754	180	35	122	0.43	13.6	22.3
352	1385	130	32	167	0.48	13.2	26.8
353	1411	131	27	156	0.39	12.4	17.5
354	1203	142	33	166	0.52	12.1	17.6
355	1015	135	23	134	0.52	12.4	27.5
MEAN	1063	124	32	141	0.49	12.5	24.5
SD	422.6	35.3	7.4	30.5	0.046	1.71	4.92
N	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)							
366	976	105	33	125	0.45	16.9	39.1
367	816	72	30	127	0.40	10.4	27.9
368	1461	109	28	156	0.52	8.3	24.0
369	1613	122	28	157	0.38	21.6	18.7
370	1375	166	34	162	0.47	9.5	23.4
371	1414	108	28	141	0.45	12.1	20.7
372	1641	107	25	161	0.73	17.0	24.8
373	731	111	44	158	0.59	31.0	22.9
374	945	136	34	127	0.55	12.3	21.4
375	805	92	22	144	0.47	10.7	22.7
MEAN	1178	113	31	146	0.50	15.0	24.6
SD	356.4	25.1	6.1	15.0	0.103	6.97	5.67
N	10	10	10	10	10	10	10

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: Mid-Low:0.55 (w/w%)							
386	1574	132	26	161	0.53	10.5	24.2
387	1260	84	24	131	0.48	10.1	23.6
388	1859	75	39	181	0.54	7.9	42.8
389	1202	77	26	155	0.37	14.9	26.1
390	936	78	27	127	0.46	11.6	22.8
391	665	88	22	97	0.40	8.1	21.4
392	1024	113	26	149	0.35	13.7	38.0
393	1848	163	33	195	0.52	11.7	18.9
394	949	169	34	148	0.46	11.7	27.3
395	796	67	27	114	0.65	13.6	19.2
MEAN	1211	105	28	146	0.48	11.4	26.4
SD	422.9	37.8	5.2	29.7	0.090	2.32	7.91
N	10	10	10	10	10	10	10
GROUP: Mid:1 (w/w%)							
406	1053	140	25	117	0.58	12.8	27.3
407	1113	189	27	111	0.43	8.8	46.9
408	897	86	29	140	0.49	19.2	26.7
409	878	107	25	144	0.52	9.2	27.1
410	889	140	26	117	0.59	8.2	47.9
411	379	94	45	119	0.59	23.3	23.1
412	1216	203	25	160	0.55	10.9	34.2
413	787	133	34	116	0.37	12.1	39.6
414	964	144	40	146	0.36	20.3	26.2
415	448	97	31	99	0.57	12.7	19.3
MEAN	862	133	31	127	0.51	13.8	31.8
SD	268.3	39.4	7.0	19.2	0.089	5.30	9.92
N	10	10	10	10	10	10	10

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: Mid-High:3 (w/w%)							
426	1576	96	38	182	0.51	15.4	31.4
427	x	x	x	x	x	x	x
428	x	x	x	x	x	x	x
429	x	x	x	x	x	x	x
430	x	x	x	x	x	x	x
431	x	x	x	x	x	x	x
432	348	176	35	117	0.41	9.5	72.4
433	x	x	x	x	x	x	x
434	x	x	x	x	x	x	x
435	x	x	x	x	x	x	x
MEAN	962	136	37	150	0.46	12.5	51.9
SD	868.3	56.6	2.1	46.0	0.071	4.17	28.99
N	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)							
446	x	x	x	x	x	x	x
447	x	x	x	x	x	x	x
448	x	x	x	x	x	x	x
449	x	x	x	x	x	x	x
450	x	x	x	x	x	x	x
451	x	x	x	x	x	x	x
452	x	x	x	x	x	x	x
453	x	x	x	x	x	x	x
454	x	x	x	x	x	x	x
455	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	CK IU/L	ALP IU/L	ALT IU/L	AST IU/L	TBIL mg/dL	SDH IU/L	TBA umol/L
GROUP: (+)Control:5 (w/w%)							
466	x	x	x	x	x	x	x
467	x	x	x	x	x	x	x
468	x	x	x	x	x	x	x
469	x	x	x	x	x	x	x
470	x	x	x	x	x	x	x
471	x	x	x	x	x	x	x
472	x	x	x	x	x	x	x
473	x	x	x	x	x	x	x
474	x	x	x	x	x	x	x
475	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: Vehicle:Distilled Water 0 (w/w%)							
346	20	0.4	100	5.4	3.8	1.6	2.4
347	23	0.5	93	5.5	3.9	1.6	2.4
348	18	0.3	96	6.0	4.2	1.8	2.3
349	22	0.4	98	5.4	3.9	1.5	2.6
350	17	0.5	113	5.6	3.9	1.7	2.3
351	23	0.6	103	5.7	4.1	1.6	2.6
352	26	0.5	73	5.6	3.9	1.7	2.3
353	19	0.6	110	5.5	4.0	1.5	2.7
354	17	0.5	87	5.0	3.5	1.5	2.3
355	21	0.5	99	5.5	4.1	1.4	2.9
MEAN	21	0.5	97	5.5	3.9	1.6	2.5
SD	3.0	0.09	11.4	0.25	0.19	0.12	0.21
N	10	10	10	10	10	10	10
GROUP: Low:0.25 (w/w%)							
366	16	0.3	104	5.8	4.3	1.5	2.9
367	21	0.6	99	5.7	4.2	1.5	2.8
368	20	0.5	100	5.8	4.4	1.4	3.1
369	14	0.5	105	5.7	3.9	1.8	2.2
370	18	0.5	85	5.4	3.8	1.6	2.4
371	16	0.4	99	5.3	3.8	1.5	2.5
372	17	0.4	101	5.4	3.9	1.5	2.6
373	21	0.5	99	5.1	3.7	1.4	2.6
374	18	0.4	86	5.1	3.7	1.4	2.6
375	20	0.4	84	5.7	4.2	1.5	2.8
MEAN	18	0.5	96	5.5	4.0	1.5	2.7
SD	2.4	0.08	8.0	0.27	0.26	0.12	0.26
N	10	10	10	10	10	10	10

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: Mid-Low:0.55 (w/w%)							
386	18	0.5	98	5.5	4.0	1.5	2.7
387	18	0.5	104	5.2	3.8	1.4	2.7
388	21	0.6	83	5.1	3.8	1.3	2.9
389	23	0.6	107	5.9	4.2	1.7	2.5
390	18	0.4	107	5.4	3.7	1.7	2.2
391	23	0.6	101	5.6	4.1	1.5	2.7
392	20	0.6	83	5.2	3.7	1.5	2.5
393	19	0.5	113	5.5	3.9	1.6	2.4
394	21	0.5	98	5.2	3.6	1.6	2.3
395	16	0.5	104	5.9	4.2	1.7	2.5
MEAN	20	0.5	100	5.5	3.9	1.6	2.5
SD	2.3	0.07	9.9	0.29	0.22	0.14	0.21
N	10	10	10	10	10	10	10
GROUP: Mid:1 (w/w%)							
406	16	0.5	92	5.3	3.8	1.5	2.5
407	19	0.5	91	5.5	4.1	1.4	2.9
408	21	0.5	100	5.0	3.6	1.4	2.6
409	20	0.6	102	5.3	3.8	1.5	2.5
410	19	0.5	95	5.6	4.0	1.6	2.5
411	24	0.5	104	5.5	3.9	1.6	2.4
412	16	0.5	84	5.4	3.9	1.5	2.6
413	19	0.5	86	5.5	3.9	1.6	2.4
414	22	0.4	81	5.4	4.1	1.3	3.2
415	17	0.4	108	5.4	4.0	1.4	2.9
MEAN	19	0.5	94	5.4	3.9	1.5	2.7
SD	2.6	0.06	9.1	0.17	0.15	0.10	0.26
N	10	10	10	10	10	10	10

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: Mid-High:3 (w/w%)							
426	19	0.5	100	5.7	4.0	1.7	2.4
427	x	x	x	x	x	x	x
428	x	x	x	x	x	x	x
429	x	x	x	x	x	x	x
430	x	x	x	x	x	x	x
431	x	x	x	x	x	x	x
432	18	0.5	97	5.1	3.5	1.6	2.2
433	x	x	x	x	x	x	x
434	x	x	x	x	x	x	x
435	x	x	x	x	x	x	x
MEAN	19	0.5	99	5.4	3.8	1.7	2.3
SD	0.7	0.00	2.1	0.42	0.35	0.07	0.14
N	2	2	2	2	2	2	2
GROUP: High:5 (w/w%)							
446	x	x	x	x	x	x	x
447	x	x	x	x	x	x	x
448	x	x	x	x	x	x	x
449	x	x	x	x	x	x	x
450	x	x	x	x	x	x	x
451	x	x	x	x	x	x	x
452	x	x	x	x	x	x	x
453	x	x	x	x	x	x	x
454	x	x	x	x	x	x	x
455	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal fated in Previous Period

Appendix I

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Terminal

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	BUN mg/dL	CREA mg/dL	GLU mg/dL	TP g/dL	ALB g/dL	GLOB g/dL	A/G -
GROUP: (+)Control:5 (w/w%)							
466	x	x	x	x	x	x	x
467	x	x	x	x	x	x	x
468	x	x	x	x	x	x	x
469	x	x	x	x	x	x	x
470	x	x	x	x	x	x	x
471	x	x	x	x	x	x	x
472	x	x	x	x	x	x	x
473	x	x	x	x	x	x	x
474	x	x	x	x	x	x	x
475	x	x	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA	NA	NA
N	0	0	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: Vehicle:Distilled Water 0 (w/w%)					
336	40	164.4	93.3	0.4	1.76
337	48	99.0	62.3	0.8	1.59
338	12	56.3	26.5	0.5	2.12
339	56	154.0	85.0	0.7	1.81
340	85	169.7	91.2	0.9	1.86
341	58	109.8	52.9	1.1	2.08
342	36	119.8	64.7	0.6	1.85
343	61	180.9	103.9	0.6	1.74
344	78	143.2	70.0	1.1	2.05
345	49	140.8	91.4	0.5	1.54
MEAN	52	133.8	74.1	0.7	1.84
SD	20.9	37.97	23.40	0.25	0.197
N	10	10	10	10	10
GROUP: Low:0.25 (w/w%)					
356	11	57.7	30.8	0.4	1.87
357	35	99.0	42.9	0.8	2.31
358	23	116.6	62.6	0.4	1.86
359	56	98.6	53.5	1.0	1.84
360	21	66.5	33.5	0.6	1.99
361	18	34.5	15.7	1.1	2.20
362	44	101.0	61.7	0.7	1.64
363	37	61.4	42.1	0.9	1.46
364	30	149.1	87.5	0.3	1.70
365	40	101.2	52.9	0.8	1.91
MEAN	32	88.6	48.3	0.7	1.88
SD	13.6	33.46	20.07	0.27	0.251
N	10	10	10	10	10

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: Mid-Low:0.55 (w/w%)					
376	51	113.6	76.4	0.7	1.49
377	42	90.1	47.2	0.9	1.91
378	16	54.3	28.6	0.6	1.90
379	40	93.6	55.7	0.7	1.68
380	41	114.5	62.5	0.7	1.83
381	37	58.0	33.1	1.1	1.75
382	41	217.4	122.6	0.3	1.77
383	80	183.7	103.9	0.8	1.77
384	57	117.5	65.4	0.9	1.80
385	51	89.1	56.7	0.9	1.57
MEAN	46	113.2	65.2	0.8	1.75
SD	16.4	51.49	29.40	0.22	0.134
N	10	10	10	10	10
GROUP: Mid:1 (w/w%)					
396	63	132.7	92.7	0.7	1.43
397	98	113.6	55.8	1.8	2.04
398	86	116.0	69.2	1.2	1.68
399	5	38.1	21.5	0.2	1.77
400	33	92.2	64.9	0.5	1.42
401	57	81.5	40.6	1.4	2.01
402	64	160.4	80.7	0.8	1.99
403	50	98.3	53.3	0.9	1.84
404	36	104.6	53.2	0.7	1.97
405	71	139.3	85.2	0.8	1.63
MEAN	56	107.7	61.7	0.9	1.78
SD	27.0	33.95	21.55	0.46	0.233
N	10	10	10	10	10

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: Mid-High:3 (w/w%)					
416	x	x	x	x	x
417	x	x	x	x	x
418	x	x	x	x	x
419	x	x	x	x	x
420	x	x	x	x	x
421	x	x	x	x	x
422	x	x	x	x	x
423	20	64.7	39.9	0.5	1.62
424	x	x	x	x	x
425	19	39.8	34.7	0.5	1.15
MEAN	20	52.3	37.3	0.5	1.39
SD	0.7	17.61	3.68	0.00	0.332
N	2	2	2	2	2
GROUP: High:5 (w/w%)					
436	x	x	x	x	x
437	x	x	x	x	x
438	x	x	x	x	x
439	x	x	x	x	x
440	x	x	x	x	x
441	x	x	x	x	x
442	x	x	x	x	x
443	x	x	x	x	x
444	x	x	x	x	x
445	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: MALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: (+)Control:5 (w/w%)					
456	x	x	x	x	x
457	x	x	x	x	x
458	x	x	x	x	x
459	x	x	x	x	x
460	x	x	x	x	x
461	x	x	x	x	x
462	x	x	x	x	x
463	x	x	x	x	x
464	x	x	x	x	x
465	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0

NA - Not Applicable

x - Animal fated in Previous Period

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Appendix J
Individual Animal Urinalysis Data

Dose Group (% w/w)	Animal Number	Urinalysis Parameters - Observations and Measurements - Male Rats																				
		Color	Clarity	Volume	RI	SG	PH	LEU	NIT	PRO	GLU	KET	UBG	BIL	BLD	Casts	EP cells	P04	NMR	MR	RBC	WBC	Sperm
1 - Vehicle Control	336	Yellow	Clear	6	1.3440	1.035	7.0	1	0	1	0	Trace	Norm	0	1	0	0	2	1	1	4-8	6-10	4
	337	Yellow	Clear	8	1.3406	1.024	7.0	Trace	+	1	0	0	Norm	0	1	0	1-3	1	3	2	0-2	0-3	4
	338	Pale Yellow	Clear	30	1.3368	1.013	7.0	0	0	Trace	0	0	Norm	0	0	0	0	1	1	1	0	0	1
	339	Yellow	Sl	9	1.3438	1.035	7.0	Trace	0	1	0	Trace	Norm	0	Trace	0	0	4	1	1	1-3	0-3	0
	340	Yellow	Clear	9	1.3462	1.042	7.0	Trace	0	Trace	0	Trace	Norm	0	Trace	0	0	4	2	1	0-2	0-3	1
	341	Yellow	Clear	12	1.3408	1.026	7.0	1	0	Trace	0	0	Norm	0	Trace	0	0	2	1	1	0	0	2
	342	Yellow	Clear	9	1.3410	1.026	7.0	Trace	0	Trace	0	0	Norm	0	Trace	0	0	3	1	1	0	0	2
	343	Yellow	Clear	5	1.3478	1.048	6.5	Trace	0	1	0	Trace	Norm	0	Trace	0	1-3	0	2	1	0-2	0-3	1
	344	Yellow	Clear	11	1.3432	1.032	7.0	Trace	0	Trace	0	0	Norm	0	Trace	0	0	4	2	2	0-2	0-3	2
	345	Yellow	Clear	9	1.3434	1.032	7.0	1	0	1	0	Trace	Norm	0	1	0	0-1	4	2	1	1-3	0-3	1
2 - TMAH (0.25)	356	Pale Yellow	Clear	19	1.3370	1.013	7.0	Trace	0	0	0	0	Norm	0	Trace	0	0	1	1	1	0	0-3	1
	357	Yellow	Clear	16	1.3392	1.019	7.0	Trace	0	0	0	0	Norm	0	Trace	0	0	2	1	1	0-2	0-3	1
	358	Yellow	Clear	11	1.3410	1.026	7.0	0	0	Trace	0	0	Norm	0	1	0	0	2	1	1	0-2	0-3	3
	359	Yellow	Clear	10	1.3394	1.021	8.0	Trace	0	Trace	0	0	Norm	0	Trace	0	0	3	1	1	0-2	0	2
	360	Pale Yellow	Clear	19	1.3376	1.014	7.0	Trace	0	Trace	0	0	Norm	0	2	0	0	1	2	1	0-2	0-3	2
	361	Pale Yellow	Clear	49	1.3350	1.006	7.0	0	0	0	0	0	Norm	0	1	0	0	0	2	1	0	0	0
	362	Yellow	Clear	15	1.3408	1.026	7.0	Trace	0	Trace	0	Trace	Norm	0	Trace	0	0	4	1	1	0-2	0-3	1
	363	Yellow	Clear	18	1.3380	1.016	7.0	0	0	Trace	0	Trace	Norm	0	2	0	0-1	2	2	1	1-3	0	2
	364	Yellow	Clear	5	1.3448	1.038	6.5	Trace	0	1	0	Trace	Norm	0	1	0	0	2	1	1	0-2	0	2
	365	Yellow	Clear	12	1.3400	1.022	7.0	Trace	0	1	0	Trace	Norm	0	1	0	1-3	4	2	2	0-2	0-3	1
3 - TMAH (0.55)	376	Yellow	Clear	10	1.3420	1.029	7.0	1	0	1	0	Trace	Norm	0	1	0	0-1	3	2	2	0-2	0-3	2
	377	Yellow	Clear	16	1.3396	1.021	7.0	Trace	0	0	0	0	Norm	0	1	0	0-1	0	1	1	0-2	0-3	2
	378	Pale Yellow	Clear	29	1.3368	1.013	7.0	0	0	0	0	0	Norm	0	Trace	0	0	1	1	1	0	0	1
	379	Yellow	Clear	12	1.3400	1.022	7.0	0	0	0	0	0	Norm	0	1	0	0	1	1	1	0-2	0	2
	380	Yellow	Clear	12	1.3410	1.026	7.0	Trace	0	0	0	0	Norm	0	Trace	0	1-3	3	2	1	0-2	0-3	2
	381	Pale Yellow	Clear	20	1.3374	1.014	7.0	Trace	0	0	0	0	Norm	0	0	0	0	2	2	2	0	0-3	3
	382	Yellow	Clear	5	1.3492	1.051	6.5	Trace	0	1	0	Trace	Norm	0	Trace	0	0	3	1	1	0-2	0-3	1
	383	Yellow	Clear	8	1.3476	1.048	7.0	1	0	1	0	Trace	Norm	0	1	0	0-1	3	1	1	1-3	0-3	2
	384	Yellow	Clear	10	1.3410	1.026	7.0	Trace	0	Trace	0	0	Norm	0	Trace	0	0	4	1	1	0	0	2
	385	Yellow	Clear	11	1.3398	1.022	7.0	Trace	0	Trace	0	0	Norm	0	4	0	0-1	2	3	2	0-2	0-3	2

Appendix J
Individual Animal Urinalysis Data

Dose Group	Animal	Urinalysis Parameters - Observations and Measurements - Male Rats																				
(% w/w)	Number	Color	Clarity	Volume	RI	SG	PH	LEU	NIT	PRO	GLU	KET	UBG	BIL	BLD	Casts	EP cells	P04	NMR	MR	RBC	WBC	Sperm
4 - TMAH	396	Yellow	Clear	5	1.3442	1.035	7.0	Trace	0	1	0	0	Norm	0	4	0	0	3	1	1	30-50	3-5	1
(1)	397	Yellow	Sl	12	1.3410	1.026	8.0	Trace	0	0	0	1	Norm	0	Trace	0	0	4	1	1	0-2	0	1
	398	Yellow	Clear	9	1.3422	1.029	7.0	Trace	0	Trace	0	Trace	Norm	0	1	0	1-3	1	2	2	1-3	0-3	1
	399	Pale Yellow	Clear	32	1.3360	1.010	7.0	0	0	0	0	0	Norm	0	Trace	0	0	0	2	2	0	0	0
	400	Yellow	Clear	12	1.3406	1.024	7.0	Trace	0	1	0	0	Norm	0	1	0	0	1	2	2	0-2	0	2
	401	Yellow	Clear	18	1.3382	1.016	8.0	0	0	0	0	0	Norm	0	Trace	0	0	3	1	1	0	0	1
	402	Yellow	Clear	8	1.3448	1.038	7.0	Trace	0	1	0	0	Norm	0	Trace	0	1-3	3	2	1	1-3	0-3	2
	403	Yellow	Clear	11	1.3398	1.022	7.0	Trace	0	0	0	0	Norm	0	Trace	0	0	4	1	1	0-2	0	2
	404	Yellow	Clear	16	1.3400	1.022	7.0	0	0	0	0	0	Norm	0	1	0	0	2	2	2	0	0	2
	405	Yellow	Clear	8	1.3442	1.035	6.5	1	0	1	0	Trace	Norm	0	2	0	1-3	1	2	2	0-2	6-10	2
5 - TMAH	423	Pale Yellow	Clear	21	1.3388	1.019	6.5	Trace	0	0	0	0	Norm	0	Trace	0	0	NR	3	2	0-2	0-3	2
(3)	425	Pale Yellow	Clear	24	1.3382	1.016	6.5	0	0	0	0	0	Norm	0	Trace	0	0	2	1	1	0	0	2

NR = Not Recorded

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: Vehicle:Distilled Water 0 (w/w%)					
346	45	118.0	63.0	0.7	1.87
347	24	94.8	55.8	0.4	1.70
348	12	36.6	28.4	0.4	1.29
349	38	129.1	69.0	0.6	1.87
350	21	99.1	62.5	0.3	1.59
351	55	148.2	79.6	0.7	1.86
352	29	99.1	75.4	0.4	1.31
353	27	83.3	40.7	0.7	2.05
354	21	72.0	37.1	0.6	1.94
355	44	80.3	44.2	1.0	1.82
MEAN	32	96.1	55.6	0.6	1.73
SD	13.4	31.34	17.27	0.21	0.258
N	10	10	10	10	10
GROUP: Low:0.25 (w/w%)					
366	--	29.4	16.4	--	1.79
367	31	119.1	58.5	0.5	2.04
368	12	47.2	24.9	0.5	1.90
369	42	85.8	44.0	1.0	1.95
370	6	63.5	34.0	0.2	1.87
371	68	107.1	60.3	1.1	1.78
372	55	161.3	72.7	0.8	2.22
373	37	109.2	62.9	0.6	1.74
374	33	67.6	39.9	0.8	1.69
375	53	86.0	41.5	1.3	2.07
MEAN	37	87.6	45.5	0.8	1.91
SD	20.0	38.41	17.90	0.34	0.167
N	9	10	10	9	10

(--) - Data Unavailable
(--) - Data Unavailable = Below Detection Limit For NA

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: Mid-Low:0.55 (w/w%)					
386	35	128.9	58.5	0.6	2.20
387	31	110.0	62.7	0.5	1.75
388	54	111.4	63.7	0.8	1.75
389	37	109.0	50.9	0.7	2.14
390	70	160.9	94.2	0.7	1.71
391	27	69.1	53.8	0.5	1.28
392	49	82.4	80.7	0.6	1.02
393	71	160.3	79.3	0.9	2.02
394	25	123.8	65.8	0.4	1.88
395	23	80.6	44.0	0.5	1.83
MEAN	42	113.6	65.4	0.6	1.76
SD	17.9	31.34	15.34	0.15	0.366
N	10	10	10	10	10
GROUP: Mid:1 (w/w%)					
406	25	75.1	33.7	0.7	2.23
407	14	78.3	38.7	0.4	2.02
408	19	41.5	22.5	0.8	1.84
409	44	81.3	38.7	1.1	2.10
410	10	66.4	35.5	0.3	1.87
411	15	51.3	30.9	0.5	1.66
412	12	93.5	51.1	0.2	1.83
413	48	47.5	39.0	1.2	1.22
414	42	83.4	53.2	0.8	1.57
415	8	39.2	34.7	0.2	1.13
MEAN	24	65.8	37.8	0.6	1.75
SD	15.3	19.45	9.01	0.36	0.359
N	10	10	10	10	10

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: Mid-High:3 (w/w%)					
426	7	46.5	21.5	0.3	2.16
427	x	x	x	x	x
428	x	x	x	x	x
429	x	x	x	x	x
430	x	x	x	x	x
431	x	x	x	x	x
432	8	24.7	15.4	0.5	1.60
433	x	x	x	x	x
434	x	x	x	x	x
435	x	x	x	x	x
MEAN	8	35.6	18.5	0.4	1.88
SD	0.7	15.41	4.31	0.14	0.396
N	2	2	2	2	2
GROUP: High:5 (w/w%)					
446	x	x	x	x	x
447	x	x	x	x	x
448	x	x	x	x	x
449	x	x	x	x	x
450	x	x	x	x	x
451	x	x	x	x	x
452	x	x	x	x	x
453	x	x	x	x	x
454	x	x	x	x	x
455	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

Appendix J
Individual Animal Urinalysis Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Urine

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	NA mmol/L	K mmol/L	CREA mg/dL	NA/CREA -	K/CREA -
GROUP: (+)Control:5 (w/w%)					
466	x	x	x	x	x
467	x	x	x	x	x
468	x	x	x	x	x
469	x	x	x	x	x
470	x	x	x	x	x
471	x	x	x	x	x
472	x	x	x	x	x
473	x	x	x	x	x
474	x	x	x	x	x
475	x	x	x	x	x
MEAN	NA	NA	NA	NA	NA
SD	NA	NA	NA	NA	NA
N	0	0	0	0	0

NA - Not Applicable

x - Animal Fated in Previous Period

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Appendix J
Individual Animal Urinalysis Data

Dose Group (% w/w)	Animal Number	Urinalysis Parameters - Observations and Measurements - Female Rats																				
		Color	Clarity	Volume	RI	SG	PH	LEU	NIT	PRO	GLU	KET	UBG	BIL	BLD	Casts	EP cells	P04	NMR	MR	RBC	WBC	Other
1 - Vehicle Control (0)	346	Yellow	Clear	5	1.3440	1.035	6.5	0	0	Trace	0	Trace	Norm	0	1	0	0	0	1	1	0	0	0
	347	Yellow	Clear	6	1.3432	1.032	6.0	0	0	0	0	0	Norm	0	0	0	3-6	0	2	1	0-2	0-3	0
	348	Pale Yellow	Clear	13	1.3386	1.018	6.0	0	0	0	0	0	Norm	0	Trace	0	1-3	0	2	2	0-2	3-5	0
	349	Yellow	Clear	5	1.3458	1.042	6.5	0	0	Trace	0	0	Norm	0	Trace	0	1-3	2	1	1	0-2	0-3	0
	350	Yellow	Clear	6	1.3438	1.035	6.5	0	0	0	0	0	Norm	0	Trace	0	0	1	2	1	0-2	0-3	0
	351	Yellow	Clear	5	1.3456	1.042	6.5	Trace	0	1	0	Trace	Norm	0	Trace	0	1-3	2	2	2	1-3	0-3	0
	352	Yellow	Clear	6	1.3468	1.045	6.0	0	0	Trace	0	0	Norm	0	Trace	0	0	0	1	1	0-2	0	0
	353	Yellow	Clear	13	1.3400	1.022	6.5	0	0	0	0	0	Norm	0	Trace	0	0	0	1	1	0-2	0	0
	354	Pale Yellow	Clear	14	1.3398	1.022	6.5	0	0	Trace	0	0	Norm	0	Trace	0	1-3	1	2	2	0-2	0-3	0
	355	Yellow	Clear	10	1.3410	1.026	6.5	0	0	0	0	0	Norm	0	Trace	0	0	0	1	1	0-2	0	0
2 - TMAH (0.25)	366	Pale Yellow	Clear	32	1.3358	1.010	6.5	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	367	Yellow	Clear	5	1.3420	1.029	7.0	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	368	Pale Yellow	Clear	21	1.3374	1.014	6.5	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	369	Yellow	Clear	12	1.3400	1.022	7.0	0	0	0	0	0	Norm	0	2	0	1-3	2	2	2	1-3	0	0
	370	Pale Yellow	Clear	15	1.3386	1.018	6.0	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	371	Yellow	Clear	7	1.3428	1.032	7.0	Trace	+	Trace	0	Trace	Norm	0	1	0	1-3	3	2	1	1-3	0-3	0
	372	Yellow	Clear	8	1.3468	1.045	6.5	Trace	0	Trace	0	Trace	Norm	0	Trace	0	1-3	3	2	2	1-3	3-5	0
	373	Yellow	Clear	6	1.3426	1.030	6.5	0	0	0	0	0	Norm	0	Trace	0	0	3	2	1	0-2	0-3	0
	374	Yellow	Clear	9	1.3406	1.024	6.0	0	0	0	0	0	Norm	0	Trace	0	0	0	1	1	0	0	0
	375	Yellow	Clear	8	1.3410	1.026	7.0	0	+	0	0	0	Norm	0	Trace	0	0	1	4	4	0-2	0-3	0
3 - TMAH (0.55)	386	Yellow	Clear	7	1.3438	1.035	6.0	0	0	0	0	0	Norm	0	Trace	0	1-3	1	1	1	0-2	0-3	0
	387	Yellow	Clear	6	1.3420	1.029	7.0	Trace	0	1	0	Trace	Norm	0	1	0	1-3	3	2	2	1-3	3-5	0
	388	Yellow	Clear	6	1.3462	1.042	6.5	0	0	Trace	0	0	Norm	0	Trace	0	0-1	3	2	2	1-3	0-3	0
	389	Yellow	Clear	10	1.3434	1.032	6.0	0	0	0	0	0	Norm	0	Trace	0	0	0	2	1	0	0	0
	390	Yellow	Clear	6	1.3478	1.048	6.0	0	0	Trace	0	0	Norm	0	Trace	0	0	0	1	1	0-2	0	0
	391	Yellow	Clear	10	1.3416	1.027	6.5	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	392	Yellow	Clear	6	1.3428	1.032	6.5	0	0	Trace	0	0	Norm	0	Trace	0	1-3	0	1	1	0-2	0-3	0
	393	Yellow	Clear	5	1.3486	1.051	6.5	0	0	1	0	Trace	Norm	0	Trace	0	1-3	0	1	1	1-3	3-5	0
	394	Yellow	Clear	7	1.3442	1.035	6.0	0	0	Trace	0	0	Norm	0	Trace	0	0	0	1	1	0-2	0	0
	395	Yellow	Clear	11	1.3402	1.022	6.5	Trace	0	0	0	0	Norm	0	Trace	0	0	1	2	1	0-2	0-3	0

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

Appendix J
Individual Animal Urinalysis Data

Dose Group (% w/w)	Animal Number	Urinalysis Parameters - Observations and Measurements - Female Rats																				
		Color	Clarity	Volume	RI	SG	PH	LEU	NIT	PRO	GLU	KET	UBG	BIL	BLD	Casts	EP cells	P04	NMR	MR	RBC	WBC	Other
4 - TMAH (1)	406	Pale Yellow	Clear	15	1.3390	1.019	6.5	0	0	0	0	0	Norm	0	Trace	0	0	0	1	1	0-2	0	0
	407	Yellow	Clear	10	1.3412	1.026	6.5	0	0	0	0	0	Norm	0	0	0	0	0	2	1	0-2	0-3	0
	408	Pale Yellow	Clear	23	1.3368	1.013	6.5	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	409	Yellow	Clear	16	1.3400	1.022	7.0	0	0	0	0	0	Norm	0	Trace	0	1-3	3	2	1	0-2	0-3	0
	410	Pale Yellow	Clear	12	1.3390	1.019	6.5	0	0	0	0	0	Norm	0	Trace	0	0	0	2	1	0-2	0	0
	411	Pale Yellow	Clear	16	1.3382	1.016	7.0	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	412	Yellow	Clear	8	1.3416	1.027	6.0	0	0	0	0	0	Norm	0	Trace	0	0	0	2	1	0-2	0	0
	413	Pale Yellow	Clear	13	1.3390	1.019	7.0	0	0	0	0	0	Norm	0	0	0	0-1	0	1	1	0-2	0-3	0
	414	Yellow	Clear	7	1.3416	1.027	6.5	0	0	0	0	0	Norm	0	Trace	0	1-3	2	3	3	0-2	0-3	0
	415	Pale Yellow	Clear	14	1.3378	1.016	6.5	0	0	0	0	0	Norm	0	Trace	0	0	0	2	2	0	0	0
5 - TMAH (3)	426	Pale Yellow	Clear	23	1.3368	1.013	6.5	0	0	0	0	0	Norm	0	0	0	0	0	1	1	0	0	0
	432	Pale Yellow	Clear	40	1.3360	1.010	6.0	0	0	0	0	0	Norm	0	Trace	0	0	1	2	2	0	0	0

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Vehicle:Distilled Water 0 (w/w%)		
336	350	3885
337	510	4193
338	520	3353
339	329	4052
340	447	3854
341	372	3513
342	441	4034
343	521	4628
344	395	3983
345	374	3864
MEAN	426	3936
SD	72.5	350.2
N	10	10
GROUP: Low:0.25 (w/w%)		
356	454	4073
357	432	3723
358	483	3914
359	419	3398
360	407	3846
361	536	4646
362	494	3758
363	467	3974
364	437	3777
365	430	3988
MEAN	456	3910
SD	39.6	319.8
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-Low:0.55 (w/w%)		
376	501	4266
377	404	3986
378	533	4288
379	451	4040
380	453	3469
381	462	4062
382	426	2947
383	462	4035
384	356	3476
385	457	4557
MEAN	451	3913
SD	48.7	478.4
N	10	10
GROUP: Mid:1 (w/w%)		
396	413	3662
397	575	3368
398	401	3217
399	432	3768
400	466	3884
401	436	4223
402	409	4021
403	424	3756
404	454	4172
405	379	4195
MEAN	439	3827
SD	54.1	344.9
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-High:3 (w/w%)		
416	459	4416
417	409	4100
418	642	4242
419	561	3977
420	400	3726
421	358	3558
422	378	3638
423	403	4396
424	399	4215
425	513	3767
MEAN	452	4004
SD	91.8	316.4
N	10	10
GROUP: High:5 (w/w%)		
436	484	3986
437	384	3699
438	466	4026
439	332	3912
440	442	3392
441	434	4139
442	a	a
443	401	4058
444	a	a
445	CL	CL
MEAN	420	3887
SD	52.1	259.1
N	7	7

CL - Clotted a - Dead

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: (+)Control:5 (w/w%)		
456	394	3999
457	463	4236
458	361	4432
459	431	3815
460	535	3479
461	459	4083
462	373	3843
463	430	4097
464	424	3993
465	523	3721
MEAN	439	3970
SD	57.8	270.3
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Vehicle;Distilled Water 0 (w/w%)		
336	342	3560
337	480	3162
338	542	3016
339	327	3667
340	463	3843
341	358	3246
342	503	3540
343	481	4301
344	419	3808
345	426	4203
MEAN	434	3635
SD	72.7	423.4
N	10	10
GROUP: Low:0.25 (w/w%)		
356	474	3953
357	481	3368
358	458	3888
359	485	3563
360	384	3784
361	595	4414
362	521	3860
363	494	3251
364	460	3762
365	452	3746
MEAN	480	3759
SD	53.8	323.8
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-Low:0.55 (w/w%)		
376	494	4349
377	428	3671
378	572	4002
379	499	3139
380	492	3292
381	473	3633
382	408	3157
383	481	3568
384	374	3834
385	472	3801
MEAN	469	3645
SD	55.0	381.3
N	10	10
GROUP: Mid:1 (w/w%)		
396	431	3298
397	626	3961
398	430	3363
399	454	3573
400	484	3667
401	490	3823
402	438	3357
403	513	3017
404	447	4084
405	366	3416
MEAN	468	3556
SD	68.7	330.0
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-High:3 (w/w%)		
416	a	a
417	a	a
418	a	a
419	a	a
420	a	a
421	a	a
422	a	a
423	419	3868
424	a	a
425	552	3694
MEAN	486	3781
SD	94.0	123.0
N	2	2
GROUP: High:5 (w/w%)		
436	a	a
437	a	a
438	a	a
439	a	a
440	a	a
441	a	a
442	x	x
443	a	a
444	x	x
445	a	a
MEAN	NA	NA
SD	NA	NA
N	0	0

NA - Not Applicable
a - Dead
x - Animal Fated in Previous Period

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: MALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: (+)Control:5 (w/w%)		
456	b	b
457	b	b
458	b	b
459	b	b
460	b	b
461	b	b
462	b	b
463	b	b
464	b	b
465	b	b
MEAN	NA	NA
SD	NA	NA
N	0	0

NA - Not Applicable

b - Terminal Sacrifice

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Vehicle:Distilled Water 0 (w/w%)		
346	607	3823
347	886	3554
348	597	3946
349	754	4210
350	829	3808
351	603	3786
352	694	4607
353	537	4275
354	545	3783
355	658	3267
MEAN	671	3906
SD	118.7	380.0
N	10	10
GROUP: Low:0.25 (w/w%)		
366	1123	3663
367	1559	4517
368	785	3940
369	627	3293
370	550	3770
371	572	3640
372	1052	3282
373	871	4011
374	573	3744
375	806	4397
MEAN	852	3826
SD	319.4	408.5
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-Low:0.55 (w/w%)		
386	604	4269
387	794	3904
388	605	3522
389	636	3921
390	787	3994
391	770	3659
392	577	4179
393	859	4179
394	621	4316
395	740	3763
MEAN	699	3971
SD	101.0	267.5
N	10	10
GROUP: Mid:1 (w/w%)		
406	615	3906
407	582	4042
408	655	3905
409	569	4129
410	838	4343
411	639	3689
412	512	4007
413	536	4546
414	548	4431
415	CL	CL
MEAN	610	4111
SD	97.6	279.3
N	9	9

CL - Clotted

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-High:3 (w/w%)		
426	742	3952
427	527	3558
428	809	4183
429	1002	4237
430	786	4181
431	1184	3601
432	824	4791
433	664	4178
434	a	a
435	a	a
MEAN	817	4085
SD	201.1	392.6
N	8	8
GROUP: High:5 (w/w%)		
446	a	a
447	a	a
448	a	a
449	a	a
450	a	a
451	a	a
452	a	a
453	933	3858
454	a	a
455	a	a
MEAN	933	3858
SD	NA	NA
N	1	1

NA - Not Applicable

a - Dead

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 2

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: (+)Control:5 (w/w%)		
466	556	4089
467	569	3781
468	527	4011
469	543	3917
470	738	4171
471	579	3977
472	653	3601
473	663	3447
474	718	4896
475	615	4324
MEAN	616	4021
SD	74.0	402.9
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Vehicle:Distilled Water 0 (w/w%)		
346	874	3725
347	1222	4008
348	985	3928
349	1246	3510
350	1240	3440
351	1422	4062
352	1454	4087
353	800	3067
354	701	3651
355	1104	3723
MEAN	1105	3720
SD	257.8	321.7
N	10	10
GROUP: Low:0.25 (w/w%)		
366	2123	3377
367	2231	4880
368	1104	3317
369	737	3233
370	713	3876
371	839	3579
372	1415	3822
373	1457	3714
374	840	3662
375	1395	3984
MEAN	1285	3744
SD	549.0	469.6
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-Low:0.55 (w/w%)		
386	1034	4195
387	914	3533
388	658	3312
389	928	3637
390	971	4302
391	1195	3393
392	816	2888
393	1460	3290
394	953	3264
395	1230	3509
MEAN	1016	3532
SD	227.9	429.1
N	10	10
GROUP: Mid:1 (w/w%)		
406	779	3316
407	990	3085
408	749	3561
409	682	4538
410	1468	3449
411	1045	4034
412	711	3782
413	990	3581
414	918	3811
415	991	4034
MEAN	932	3719
SD	230.6	416.7
N	10	10

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: Mid-High:3 (w/w%)		
426	1012	3507
427	a	a
428	a	a
429	a	a
430	a	a
431	a	a
432	800	3889
433	a	a
434	x	x
435	x	x
MEAN	906	3698
SD	149.9	270.1
N	2	2
GROUP: High:5 (w/w%)		
446	x	x
447	x	x
448	x	x
449	x	x
450	x	x
451	x	x
452	x	x
453	a	a
454	x	x
455	x	x
MEAN	NA	NA
SD	NA	NA
N	0	0

NA - Not Applicable
a - Dead
x - Animal Fated in Previous Period

Appendix K
Individual Animal Acetylcholinesterase Data

INDIVIDUAL ANIMAL CLINICAL CHEMISTRY DATA
PERIOD: Day 24

STUDY ID: 1052SN3 SEX: FEMALE

Animal ID	PCHE(C) U/L	ECHE U/L
GROUP: (+)Control:5 (w/w%)		
466	b	b
467	b	b
468	b	b
469	b	b
470	b	b
471	b	b
472	b	b
473	b	b
474	b	b
475	b	b
MEAN	NA	NA
SD	NA	NA
N	0	0

NA - Not Applicable b - Terminal Sacrifice

Appendix L
Individual Animal Blood Gas Data

Dose Group (% w/w)	Sex	Animal	Parameter			
			pH	PCO_2	PO_2	HCO_3
Vehicle Control (0)	M	1	7.261	59.4	165	27.0
	M	2	7.228	58.6	234	24.7
	M	3	7.231	64.7	228	27.5
	M	4	7.256	61.6	200	27.7
	M	5	7.258	55.6	219	25.1
	M	6	7.258	57.8	162	26.1
TMAH (5)	M	13	7.218	66.5	121	27.4
	M	14	7.281	53.3	165	25.1
	M	15	7.254	59.7	140	26.7
	M	16	7.271	56.4	165	26.2
	M	17	7.257	58.8	147	26.5
	M	18	7.275	55.6	128	26.1
TMAH (25)	M	25	--[a]	--	--	--
	M	26	6.979	101.2	155	24.1
	M	27	7.016	83.6	206	21.6
	M	28	6.981	110.0	182	26.2
	M	29	7.016	95.3	272	24.6
	M	30	7.059	82.4	256	23.5
TMAH (25)[b]	M	1421	7.260	55.3	152	25.1
	M	1426	7.271	58.3	178	27.1

[a] -- = No data, clotted sample
[b] Extra rats; data not used in statistical analysis
Gas units (PCO_2, PO_2, HCO_3) = mmHg

Appendix L
Individual Animal Blood Gas Data

Dose Group (% w/w)	Sex	Animal	Parameter			
			pH	PCO_2	PO_2	HCO_3
Vehicle Control (0)	F	7	7.164	64.7	258	23.5
	F	8	7.267	58.3	278	26.9
	F	9	7.283	52.2	196	24.9
	F	10	7.267	57.3	272	26.4
	F	11	7.266	56.2	167	25.9
	F	12	7.266	57.9	172	26.6
TMAH (5)	F	19	7.195	68.2	148	26.6
	F	20	7.254	59.8	139	26.8
	F	21	7.271	50.3	159	23.4
	F	22	7.237	57.8	165	24.8
	F	23	7.275	54.0	170	25.3
	F	24	7.225	59.3	173	24.8
TMAH (25)	F	31	6.950	106.8	171	23.7
	F	32	--[a]	--	--	--
	F	33	7.016	96.6	222	25.0
	F	34	6.946	95.4	250	21.0
	F	35	6.928	112.1	214	23.7
	F	36	6.944	104.8	134	23.0
TMAH (25)[b]	F	1444	6.935	98.5	93	21.1
	F	1457	7.045	87.8	83	24.2

[a] -- = No data, clotted sample
[b] Extra rats; data not used in statistical analysis
Gas units (PCO_2, PO_2, HCO_3) = mmHg

Appendix M
Individual Hematology Data - Blood Gas Animals

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: MALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Control:DI Water									
1	6.4	5.75	12.3	35.0	37	60.8	21.4	35.1	975
2	3.9	5.40	12.5	35.2	37	65.2	23.1	35.5	1013
3	5.9	5.37	12.3	34.0	37	63.4	22.9	36.2	1291
4	4.9	5.22	11.8	32.7	35	62.7	22.6	36.1	1095
5	8.7	5.34	12.7	35.1	38	65.8	23.8	36.2	1045
6	5.2	5.64	12.8	35.4	38	62.8	22.7	36.2	991
MEAN	5.8	5.45	12.4	34.6	37	63.5	22.8	35.9	1068
SD	1.65	0.200	0.36	1.04	1.1	1.82	0.79	0.47	117.1
N	6	6	6	6	6	6	6	6	6
GROUP: 5%:TMAH									
13	4.8	5.37	12.4	33.5	36	62.4	23.1	37.0	958
14	3.9	5.82	12.5	35.2	38	60.5	21.5	35.5	1247
15	4.6	5.64	12.5	35.3	37	62.5	22.2	35.4	1023
16	5.0	5.26	12.0	32.8	35	62.3	22.8	36.6	1173
17	7.0	5.56	12.4	34.3	36	61.7	22.3	36.2	1265
18	6.5	5.96	12.9	36.9	39	61.9	21.6	35.0	1103
MEAN	5.3	5.60	12.5	34.7	37	61.9	22.3	36.0	1128
SD	1.19	0.264	0.29	1.46	1.5	0.74	0.63	0.77	122.9
N	6	6	6	6	6	6	6	6	6
GROUP: 25%:TMAH									
25	CL	CL	CL	CL	CL	CL	CL	CL	CL
26	2.1	5.54	12.7	35.5	37	64.1	22.9	35.8	1005
27	9.6	5.53	13.2	36.1	36	65.3	23.9	36.6	914
28	3.5	5.85	13.0	36.7	39	62.7	22.2	35.4	973
29	7.3	5.54	12.5	35.1	37	63.4	22.6	35.6	1003
30	7.9	5.90	13.2	36.0	37	61.1	22.4	36.7	1030
MEAN	6.1	5.67	12.9	35.9	37	63.3	22.8	36.0	985
SD	3.15	0.186	0.31	0.61	1.1	1.57	0.67	0.59	44.5
N	5	5	5	5	5	5	5	5	5

WBC corrected for NRBC > 0

CL - Clotted

Appendix M
Individual Hematology Data - Blood Gas Animals

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: MALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Control:DI Water									
1	10.1	580.8	0	0.9	5.3	0.1	0.1	0.0	0.0
2	10.7	577.8	0	0.5	3.4	0.0	0.0	0.0	0.0
3	12.3	660.5	0	0.4	5.3	0.2	0.1	0.0	0.0
4	8.8	459.4	0	0.5	4.4	0.0	0.0	0.0	0.0
5	11.5	614.1	0	0.7	8.0	0.0	0.0	0.0	0.0
6	6.0	338.4	0	0.6	4.4	0.2	0.1	0.0	0.0
MEAN	9.9	538.5	0.0	0.6	5.1	0.1	0.1	0.0	0.0
SD	2.25	118.52	0.00	0.18	1.57	0.10	0.05	0.00	0.00
N	6	6	6	6	6	6	6	6	6
GROUP: 5%:TMAH									
13	8.4	451.1	0	0.7	4.0	0.1	0.0	0.0	0.0
14	11.6	675.1	0	0.6	3.3	0.0	0.0	0.0	0.0
15	7.2	406.1	0	0.4	4.2	0.0	0.0	0.0	0.0
16	9.0	473.4	0	0.4	4.5	0.1	0.0	0.0	0.0
17	8.9	494.8	0	0.9	6.0	0.1	0.0	0.0	0.0
18	6.1	363.6	0	0.5	5.9	0.1	0.0	0.0	0.0
MEAN	8.5	477.4	0.0	0.6	4.7	0.1	0.0	0.0	0.0
SD	1.87	107.82	0.00	0.19	1.08	0.05	0.00	0.00	0.00
N	6	6	6	6	6	6	6	6	6
GROUP: 25%:TMAH									
25	CL	CL	CL	--	--	--	--	--	--
26	9.8	542.9	0	0.3	1.8	0.0	0.0	0.0	0.0
27	8.5	470.0	2	1.2	8.4	0.1	0.0	0.0	0.0
28	10.0	585.0	0	0.5	2.9	0.1	0.0	0.0	0.0
29	16.2	897.5	0	1.3	5.8	0.1	0.1	0.0	0.0
30	11.5	678.5	0	0.9	6.7	0.3	0.0	0.0	0.0
MEAN	11.2	634.8	0.4	0.8	5.1	0.1	0.0	0.0	0.0
SD	2.99	165.08	0.89	0.43	2.72	0.11	0.04	0.00	0.00
N	5	5	5	5	5	5	5	5	5

WBC corrected for NRBC > 0
CL - Clotted
(--) - Data Unavailable

Appendix M
Individual Hematology Data - Blood Gas Animals

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: FEMALE

Animal ID	WBC thsn/cmm	RBC mill/cmm	HGB g/dL	HCT %	PCV %	MCV fl	MCH pg	MCHC %	PLT thsn/cmm
GROUP: Control:DI Water									
7	4.7	5.30	12.0	33.7	36	63.6	22.6	35.6	1411
8	4.6	5.14	11.8	32.0	34	62.2	23.0	36.9	1182
9	6.2	4.97	10.9	29.6	32	59.5	21.9	36.8	1292
10	2.8	5.31	11.5	32.5	35	61.2	21.7	35.4	821
11	5.0	5.14	11.8	32.5	35	63.2	23.0	36.3	1217
12	4.8	5.48	11.8	33.4	36	61.0	21.5	35.3	1066
MEAN	4.7	5.22	11.6	32.3	35	61.8	22.3	36.1	1165
SD	1.08	0.177	0.39	1.46	1.5	1.53	0.67	0.71	203.9
N	6	6	6	6	6	6	6	6	6
GROUP: 5%:TMAH									
19	4.6	5.06	11.6	32.5	35	64.2	22.9	35.7	1199
20	3.2	5.37	12.4	33.6	36	62.5	23.1	36.9	1248
21	5.4	5.40	12.6	34.2	37	63.3	23.3	36.8	1266
22	4.8	5.15	12.1	32.5	35	63.2	23.5	37.2	1240
23	4.2	5.40	12.5	34.6	37	64.1	23.1	36.1	1218
24	3.7	5.16	12.0	32.1	34	62.3	23.3	37.4	1138
MEAN	4.3	5.26	12.2	33.3	36	63.3	23.2	36.7	1218
SD	0.79	0.151	0.37	1.03	1.2	0.79	0.21	0.66	45.7
N	6	6	6	6	6	6	6	6	6
GROUP: 25%:TMAH									
31	3.7	5.34	12.3	33.7	36	63.1	23.0	36.5	1073
32	CL	CL	CL	CL	CL	CL	CL	CL	CL
33	3.7	5.63	12.6	35.2	37	62.5	22.4	35.8	1055
34	CL	CL	CL	CL	CL	CL	CL	CL	CL
35	4.1	4.58	11.2	29.7	32	64.8	24.5	37.7	1086
36	11.1	5.17	12.1	34.2	36	66.2	23.4	35.4	1096
MEAN	5.7	5.18	12.1	33.2	35	64.1	23.3	36.3	1078
SD	3.63	0.443	0.60	2.42	2.2	1.68	0.88	1.01	17.7
N	4	4	4	4	4	4	4	4	4

WBC corrected for NRBC > 0

CL - Clotted

Appendix M
Individual Hematology Data - Blood Gas Animals

INDIVIDUAL ANIMAL HEMATOLOGY DATA
PERIOD: 1-3 Hour

STUDY ID: 1052_3 SEX: FEMALE

Animal ID	RETPC %	RETABS thsn/cmm	NRBC #/100 WBC	MAT NEU thsn/cmm	LYMPH thsn/cmm	MONO thsn/cmm	EOSIN thsn/cmm	BASO thsn/cmm	IMM NEU thsn/cmm
GROUP: Control:DI Water									
7	14.2	752.6	0	0.5	4.0	0.2	0.0	0.0	0.0
8	9.3	478.0	0	0.5	4.1	0.0	0.0	0.0	0.0
9	8.3	412.5	0	1.0	5.1	0.1	0.1	0.0	0.0
10	9.2	488.5	2	0.1	2.7	0.1	0.0	0.0	0.0
11	10.1	519.1	0	0.9	4.0	0.0	0.1	0.0	0.0
12	8.3	454.8	0	0.8	4.0	0.0	0.0	0.0	0.0
MEAN	9.9	517.6	0.3	0.6	4.0	0.1	0.0	0.0	0.0
SD	2.21	120.53	0.82	0.33	0.76	0.08	0.05	0.00	0.00
N	6	6	6	6	6	6	6	6	6
GROUP: 5%:TMAH									
19	8.4	425.0	0	0.6	4.0	0.0	0.0	0.0	0.0
20	7.5	402.8	0	0.4	2.8	0.0	0.0	0.0	0.0
21	9.3	502.2	0	0.5	4.7	0.1	0.1	0.0	0.0
22	7.6	391.4	0	0.5	4.2	0.0	0.0	0.0	0.0
23	5.9	318.6	0	0.5	3.6	0.1	0.0	0.0	0.0
24	6.4	330.2	0	0.4	3.2	0.0	0.0	0.0	0.0
MEAN	7.5	395.0	0.0	0.5	3.8	0.0	0.0	0.0	0.0
SD	1.25	67.08	0.00	0.08	0.69	0.05	0.04	0.00	0.00
N	6	6	6	6	6	6	6	6	6
GROUP: 25%:TMAH									
31	7.6	405.8	0	0.3	3.4	0.0	0.0	0.0	0.0
32	CL	CL	CL	--	--	--	--	--	--
33	12.5	703.8	2	0.4	3.3	0.0	0.0	0.0	0.0
34	CL	CL	CL	--	--	--	--	--	--
35	9.9	453.4	0	0.3	3.7	0.0	0.0	0.0	0.0
36	9.0	465.3	0	0.9	10.2	0.0	0.0	0.0	0.0
MEAN	9.8	507.1	0.5	0.5	5.2	0.0	0.0	0.0	0.0
SD	2.06	133.65	1.00	0.29	3.37	0.00	0.00	0.00	0.00
N	4	4	4	4	4	4	4	4	4

WBC corrected for NRBC > 0
(--) - Data Unavailable
CL - Clotted

Appendix N
Individual Red Blood Cell Morphology Observations - Blood Gas Animals

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052_3

SEX: MALE

GROUP: Control : DI Water

Animal ID	1-3 Hour
1	Polychromasia ++; Anisocytosis +; Platelets Adequate and Normal
2	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Adequate and Normal
3	Polychromasia ++; Anisocytosis ++; Poikilocytosis +; Hypochromia +; Platelets Increased and Normal
4	Polychromasia ++; Anisocytosis ++; Target Cells ++; Platelets Adequate and Normal
5	Polychromasia ++; Anisocytosis ++; Target Cells +; Platelets Adequate and Normal
6	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal

Appendix N
Individual Red Blood Cell Morphology Observations - Blood Gas Animals

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052_3 SEX: MALE

GROUP: 5% : TMAH

Animal ID	1-3 Hour
13	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Adequate and Normal
14	Polychromasia ++; Anisocytosis ++; Platelets Adequate and Normal
15	Polychromasia ++; Anisocytosis ++; Target Cells +; Platelets Adequate and Normal
16	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Adequate and Normal
17	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Increased and Normal
18	Polychromasia +; Anisocytosis +; Target Cells +; Platelets Adequate and Normal

Appendix N
Individual Red Blood Cell Morphology Observations - Blood Gas Animals

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052_3 SEX: MALE

GROUP: 25% : TMAH

Animal ID	1-3 Hour
25	--
26	Polychromasia ++; Anisocytosis +; Platelets Adequate and Normal
27	Polychromasia ++; Anisocytosis +; Target Cells +; Macrocytosis +; Platelets Adequate and Normal
28	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
29	Polychromasia ++; Anisocytosis +; Platelets Adequate and Normal
30	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Adequate and Normal

(--) - Data Unavailable

Appendix N
Individual Red Blood Cell Morphology Observations - Blood Gas Animals

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052_3 SEX: FEMALE

GROUP: Control : DI Water

Animal ID	1-3 Hour
7	Polychromasia ++; Anisocytosis ++; Target Cells +; Platelets Increased and Normal
8	Polychromasia ++; Anisocytosis ++; Target Cells +; Platelets Adequate and Normal
9	Anisocytosis ++; Anisocytosis +; Hypochromia +; Platelets Increased and Normal
10	Polychromasia ++; Anisocytosis ++; Target Cells +; Microcytosis +; Hypochromia +; Platelets Adequate and Normal
11	Polychromasia ++; Anisocytosis +; Platelets Adequate and Normal
12	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Adequate and Normal

Appendix N
Individual Red Blood Cell Morphology Observations - Blood Gas Animals

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052_3 SEX: FEMALE

GROUP: 5% : TMAH

Animal ID	1-3 Hour
19	Polychromasia +; Anisocytosis +; Target Cells +; Platelets Adequate and Normal
20	Polychromasia +; Anisocytosis +; Platelets Increased and Normal
21	Polychromasia ++; Anisocytosis ++; Target Cells +; Platelets Adequate and Normal
22	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
23	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
24	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal

Appendix N
Individual Red Blood Cell Morphology Observations - Blood Gas Animals

INDIVIDUAL RED BLOOD CELL MORPHOLOGY OBSERVATIONS

STUDY ID: 1052_3 SEX: FEMALE

GROUP: 25% : TMAH

Animal ID	1-3 Hour
31	Polychromasia +; Anisocytosis +; Platelets Adequate and Normal
32	--
33	Polychromasia ++; Anisocytosis +; Platelets Adequate and Normal
34	--
35	Polychromasia ++; Anisocytosis +; Platelets Adequate and Normal
36	Polychromasia ++; Anisocytosis +; Target Cells +; Platelets Adequate and Normal

(--) - Data Unavailable

Appendix O
Individual Absolute Organ Weight Data

Dose Group (% w/w)	Animal Number	Body Weight (g)	Absolute Organ Weight (g) - Male Rats						
			Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes
1 - Vehicle Control	336	333	0.067	2.05	1.46	2.93	13.33	0.91	2.90
	337	305	0.064	2.02	1.26	2.60	9.27	0.75	4.04
	338	330	0.089	2.07	1.18	2.55	9.06	0.64	3.15
	339	310	0.076	1.94	1.20	2.43	8.58	0.66	3.04
	340	348	0.070	1.99	1.37	3.02	10.42	0.92	2.84
	341	303	0.060	2.11	1.14	2.70	9.82	0.51	3.23
	342	304	0.089	1.91	1.33	2.49	8.14	0.52	3.12
	343	319	0.067	1.98	1.46	2.68	8.95	0.57	3.40
	344	332	0.082	2.04	1.51	2.67	9.43	0.77	3.23
	345	344	0.063	2.04	1.36	2.53	9.77	0.63	3.36
2 - TMAH (0.25)	356	321	0.074	2.02	1.08	2.65	9.91	0.67	3.32
	357	318	0.061	1.93	1.34	2.60	9.55	0.69	3.21
	358	291	0.074	2.04	1.24	2.41	7.95	0.62	3.34
	359	296	0.067	2.01	1.30	2.60	8.19	0.58	3.39
	360	327	0.078	2.30	1.20	2.75	8.98	0.69	3.48
	361	321	0.081	2.08	1.45	3.11	9.69	0.66	3.46
	362	334	0.079	1.94	1.27	2.59	8.51	0.70	3.19
	363	297	0.058	2.01	1.24	2.36	8.19	0.72	3.30
	364	335	0.068	2.01	1.30	3.01	9.37	0.75	3.00
	365	319	0.088	2.07	1.35	2.52	9.40	0.73	3.92
3 - TMAH (0.55)	376	333	0.082	2.00	1.21	2.67	11.52	0.79	3.16
	377	319	0.064	1.98	1.06	2.89	9.88	0.57	2.86
	378	366	0.062	2.01	1.50	2.68	10.16	0.83	3.27
	379	322	0.059	2.01	1.12	2.71	9.78	0.67	3.31
	380	317	0.058	1.93	1.13	2.48	8.43	0.56	3.08
	381	328	0.079	2.10	1.34	2.80	9.23	0.63	3.43
	382	332	0.088	2.06	1.34	2.88	9.91	0.58	3.27
	383	341	0.064	1.87	1.21	2.62	9.41	0.75	3.45
	384	315	0.083	2.00	1.33	2.83	9.74	0.63	3.51
	385	296	0.061	2.06	1.28	2.53	8.02	0.66	3.04
4 - TMAH (1)	396	293	0.052	1.99	1.25	2.26	8.10	0.58	3.22
	397	330	0.068	1.89	1.35	2.66	9.07	0.70	3.59
	398	298	0.080	2.10	1.10	2.48	8.18	0.70	3.36
	399	298	0.085	2.07	1.18	2.56	9.44	0.48	3.47
	400	345	0.065	2.06	1.36	2.89	9.70	0.63	3.25
	401	332	0.060	2.05	1.38	2.85	8.83	0.75	3.77
	402	298	0.084	2.05	1.16	2.78	8.29	0.54	3.08
	403	303	0.078	2.01	1.20	2.83	9.27	0.73	2.85
	404	328	0.092	2.02	1.20	2.63	9.95	0.65	3.51
	405	319	0.066	1.97	1.11	2.47	9.02	0.68	3.27
5 - TMAH (3)	423	319	0.042	1.96	1.20	2.69	9.81	0.66	3.36
	425	336	0.069	2.13	1.43	2.94	9.22	0.72	3.20

Appendix O
Individual Absolute Organ Weight Data

Dose Group (% w/w)	Animal Number	Body Weight (g)	Absolute Organ Weight (g) - Female Rats						
			Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen
1 - Vehicle Control	346	217	0.068	1.91	0.89	1.90	7.61	0.111	0.58
	347	196	0.072	2.01	0.69	1.85	8.17	0.074	0.46
	348	197	0.080	1.92	0.87	1.76	6.30	0.078	0.49
	349	227	0.057	2.00	0.89	1.97	6.87	0.094	0.52
	350	220	0.068	1.99	1.00	1.81	6.78	0.095	0.46
	351	209	0.058	2.04	0.85	1.85	6.06	0.093	0.45
	352	214	0.063	1.93	0.82	1.60	6.91	0.107	0.60
	353	240	0.073	1.96	0.93	2.21	8.85	0.163	0.69
	354	209	0.076	1.97	0.83	1.86	6.39	0.118	0.53
	355	196	0.068	1.91	0.87	1.77	6.33	0.126	0.44
2 - TMAH (0.25)	366	220	0.087	1.76	0.89	2.00	7.12	0.119	0.56
	367	202	0.080	2.00	1.00	1.83	6.75	0.101	0.54
	368	220	0.060	1.91	0.93	1.76	6.72	0.088	0.44
	369	221	0.084	1.98	0.88	1.85	7.21	0.122	0.51
	370	206	0.062	2.05	0.99	1.88	6.47	0.097	0.53
	371	199	0.078	1.74	0.80	1.73	8.17	0.126	0.51
	372	233	0.046	1.97	0.94	2.15	8.01	0.085	0.60
	373	207	0.064	1.84	0.85	1.72	6.15	0.127	0.54
	374	198	0.070	1.80	0.88	1.76	6.42	0.082	0.54
	375	185	0.070	1.78	0.86	1.81	5.64	0.101	0.46
3 - TMAH (0.55)	386	208	0.072	1.97	0.93	1.85	6.33	0.047	0.45
	387	195	0.050	1.91	0.86	1.68	6.33	0.086	0.47
	388	207	0.053	1.98	0.87	1.81	8.92	0.075	0.75
	389	223	0.073	1.82	0.93	2.08	7.03	0.116	0.40
	390	211	0.069	1.89	0.93	1.83	7.02	0.123	0.67
	391	229	0.062	1.87	0.94	1.96	6.83	0.085	0.64
	392	225	0.073	1.92	0.91	1.74	6.81	0.111	0.60
	393	188	0.065	1.95	1.00	1.75	6.26	0.097	0.56
	394	196	0.061	1.90	0.85	1.92	5.46	0.107	0.55
	395	216	0.087	1.86	0.91	1.83	7.25	0.152	0.58
4 - TMAH (1)	406	219	0.065	1.88	0.94	1.96	6.57	0.114	0.64
	407	233	0.071	2.07	0.96	1.81	6.48	0.102	0.48
	408	215	0.077	1.99	0.86	1.83	6.02	0.113	0.49
	409	234	0.081	1.94	0.96	1.92	7.22	0.113	0.54
	410	217	0.075	1.81	0.82	1.93	6.81	0.147	0.53
	411	185	0.063	1.62	0.74	1.47	5.89	0.126	0.45
	412	204	0.082	1.91	0.86	1.94	6.63	0.105	0.46
	413	227	0.079	2.03	1.06	2.28	7.73	0.084	0.54
	414	195	0.080	1.97	0.77	1.83	6.23	0.102	0.40
	415	218	0.074	1.93	0.89	2.04	8.14	0.151	0.53
5 - TMAH (3)	426	233	0.091	1.89	1.08	2.03	7.25	0.153	0.46
	432	234	0.091	1.84	0.99	1.74	7.23	0.101	0.53

Appendix P
Individual Relative[a] Organ Weight Data

Dose Group (% w/w)	Animal Number	Relative Organ Weight (%) - Male Rats						
		Adrenals	Brain	Heart	Kidneys	Liver	Spleen	Testes
1 - Vehicle Control	336	0.020	0.616	0.438	0.880	4.003	0.273	0.871
	337	0.021	0.662	0.413	0.852	3.039	0.246	1.325
	338	0.027	0.627	0.358	0.773	2.745	0.194	0.955
	339	0.025	0.626	0.387	0.784	2.768	0.213	0.981
	340	0.020	0.572	0.394	0.868	2.994	0.264	0.816
	341	0.020	0.696	0.376	0.891	3.241	0.168	1.066
	342	0.029	0.628	0.438	0.819	2.678	0.171	1.026
	343	0.021	0.621	0.458	0.840	2.806	0.179	1.066
	344	0.025	0.614	0.455	0.804	2.840	0.232	0.973
	345	0.018	0.593	0.395	0.735	2.840	0.183	0.977
2 - TMAH (0.25)	356	0.023	0.629	0.336	0.826	3.087	0.209	1.034
	357	0.019	0.607	0.421	0.818	3.003	0.217	1.009
	358	0.025	0.701	0.426	0.828	2.732	0.213	1.148
	359	0.023	0.679	0.439	0.878	2.767	0.196	1.145
	360	0.024	0.703	0.367	0.841	2.746	0.211	1.064
	361	0.025	0.648	0.452	0.969	3.019	0.206	1.078
	362	0.024	0.581	0.380	0.775	2.548	0.210	0.955
	363	0.020	0.677	0.418	0.795	2.758	0.242	1.111
	364	0.020	0.600	0.388	0.899	2.797	0.224	0.896
	365	0.028	0.649	0.423	0.790	2.947	0.229	1.229
3 - TMAH (0.55)	376	0.025	0.601	0.363	0.802	3.459	0.237	0.949
	377	0.020	0.621	0.332	0.906	3.097	0.179	0.897
	378	0.017	0.549	0.410	0.732	2.776	0.227	0.893
	379	0.018	0.624	0.348	0.842	3.037	0.208	1.028
	380	0.018	0.609	0.356	0.782	2.659	0.177	0.972
	381	0.024	0.640	0.409	0.854	2.814	0.192	1.046
	382	0.027	0.620	0.404	0.867	2.985	0.175	0.985
	383	0.019	0.548	0.355	0.768	2.760	0.220	1.012
	384	0.026	0.635	0.422	0.898	3.092	0.200	1.114
	385	0.021	0.696	0.432	0.855	2.709	0.223	1.027
4 - TMAH (1)	396	0.018	0.679	0.427	0.771	2.765	0.198	1.099
	397	0.021	0.573	0.409	0.806	2.748	0.212	1.088
	398	0.027	0.705	0.369	0.832	2.745	0.235	1.128
	399	0.029	0.695	0.396	0.859	3.168	0.161	1.164
	400	0.019	0.597	0.394	0.838	2.812	0.183	0.942
	401	0.018	0.617	0.416	0.858	2.660	0.226	1.136
	402	0.028	0.688	0.389	0.933	2.782	0.181	1.034
	403	0.026	0.663	0.396	0.934	3.059	0.241	0.941
	404	0.028	0.616	0.366	0.802	3.034	0.198	1.070
	405	0.021	0.618	0.348	0.774	2.828	0.213	1.025
5 - TMAH (3)	423	0.013	0.614	0.376	0.843	3.075	0.207	1.053
	425	0.021	0.634	0.426	0.875	2.744	0.214	0.952

[a] Relative Organ Weight = [Organ Weight (g) ÷ Body Weight (g)] x 100

Appendix P
Individual Relative[a] Organ Weight Data

Dose Group (% w/w)	Animal Number	Relative Organ Weight (%) - Female Rats						
		Adrenals	Brain	Heart	Kidneys	Liver	Ovaries	Spleen
1 - Vehicle Control	346	0.031	0.880	0.410	0.876	3.507	0.051	0.267
	347	0.037	1.026	0.352	0.944	4.168	0.038	0.235
	348	0.041	0.975	0.442	0.893	3.198	0.040	0.249
	349	0.025	0.881	0.392	0.868	3.026	0.041	0.229
	350	0.031	0.905	0.455	0.823	3.082	0.043	0.209
	351	0.028	0.976	0.407	0.885	2.900	0.045	0.215
	352	0.029	0.902	0.383	0.748	3.229	0.050	0.280
	353	0.030	0.817	0.388	0.921	3.688	0.068	0.288
	354	0.036	0.943	0.397	0.890	3.057	0.056	0.254
	355	0.035	0.974	0.444	0.903	3.230	0.064	0.224
2 - TMAH (0.25)	366	0.040	0.800	0.405	0.909	3.236	0.054	0.255
	367	0.040	0.990	0.495	0.906	3.342	0.050	0.267
	368	0.027	0.868	0.423	0.800	3.055	0.040	0.200
	369	0.038	0.896	0.398	0.837	3.262	0.055	0.231
	370	0.030	0.995	0.481	0.913	3.141	0.047	0.257
	371	0.039	0.874	0.402	0.869	4.106	0.063	0.256
	372	0.020	0.845	0.403	0.923	3.438	0.036	0.258
	373	0.031	0.889	0.411	0.831	2.971	0.061	0.261
	374	0.035	0.909	0.444	0.889	3.242	0.041	0.273
	375	0.038	0.962	0.465	0.978	3.049	0.055	0.249
3 - TMAH (0.55)	386	0.035	0.947	0.447	0.889	3.043	0.023	0.216
	387	0.026	0.979	0.441	0.862	3.246	0.044	0.241
	388	0.026	0.957	0.420	0.874	4.309	0.036	0.362
	389	0.033	0.816	0.417	0.933	3.152	0.052	0.179
	390	0.033	0.896	0.441	0.867	3.327	0.058	0.318
	391	0.027	0.817	0.410	0.856	2.983	0.037	0.279
	392	0.032	0.853	0.404	0.773	3.027	0.049	0.267
	393	0.035	1.037	0.532	0.931	3.330	0.052	0.298
	394	0.031	0.969	0.434	0.980	2.786	0.055	0.281
	395	0.040	0.861	0.421	0.847	3.356	0.070	0.269
4 - TMAH (1)	406	0.030	0.858	0.429	0.895	3.000	0.052	0.292
	407	0.030	0.888	0.412	0.777	2.781	0.044	0.206
	408	0.036	0.926	0.400	0.851	2.800	0.053	0.228
	409	0.035	0.829	0.410	0.821	3.085	0.048	0.231
	410	0.035	0.834	0.378	0.889	3.138	0.068	0.244
	411	0.034	0.876	0.400	0.795	3.184	0.068	0.243
	412	0.040	0.936	0.422	0.951	3.250	0.051	0.225
	413	0.035	0.894	0.467	1.004	3.405	0.037	0.238
	414	0.041	1.010	0.395	0.938	3.195	0.052	0.205
	415	0.034	0.885	0.408	0.936	3.734	0.069	0.243
5 - TMAH (3)	426	0.039	0.811	0.464	0.871	3.112	0.066	0.197
	432	0.039	0.786	0.423	0.744	3.090	0.043	0.227

[a] Relative Organ Weight = [Organ Weight (g) ÷ Body Weight (g)] x 100

Appendix Q - Clinical Pathology Methods

Clinical Chemistry: Beckman Synchron CX5 Methods. The following list summarizes the routine clinical chemistries available, the method used, its journal reference, and a reagent source with its catalog number:

Parameter	Method and Reference	Abbreviation
Blood Urea Nitrogen	UV-Rate Tiffany TO, *et al.*: Clin. Chem. **18**:829, 1972 Beckman Instruments, Inc. Cat. No. 442750	BUN
Calcium	Arsenazo III Michaylova V: Anal. Chim. Acta. **53**:194, 1971 Beckman Instruments, Inc. Cat. No. 442755	Ca
Cholesterol	Enzymatic Allain C.C., *et al.*: Clin. Chem **20**:470, 1974 Beckman Instruments, Inc. Cat. No. 467825	CHOL
Creatine Kinase	Rosalki Rosalki, SB: J. Lab. Clin. Med. **69**:696, 1967 Beckman Instruments, Inc. Cat. No. 442635	CK
Creatinine	Rate-Jaffe Vasiliades, J.: Clin. Chem. Acta. **22**:1664, 1976 Beckman Instruments, Inc. Cat. No. 442760	CREA or CREAT
Glucose	Hexokinase-UV Gochman, N. *et al.*: Clin. Chem. **21**:356, 1975 Beckman Instruments, Inc. Cat. No. 442640	GLU
Inorganic Phosphorus	Phosphomolybdate-UV Dryer, R.L., Routh, J.I.: Clin. Chem. **4**:191, 1963 Beckman Instruments, Inc. Cat. No. 442790	PHOS or PO4
Total Bilirubin	Jendrassik-Grof Malloy, H.T. and Evelyn, K.A.: J. Biol. Chem. **119**:481, 1937 Jendrassik, L. and Grof, P.: Biochem. Z. **297**:81, 1937 Beckman Instruments, Inc. Cat. No. 442745	TBIL
Total Protein	Biuret Hiller, A., Plazin, J., and Van Slyke, D.D.: J. Biol. Chem. **176**:1401, 1948 Beckman Instruments, Inc. Cat. No. 442740	TP or T PRO

Parameter	Method and Reference	Abbreviation
Triglycerides	Enzymatic (GPO-Trinder) Buccolo, G., and David, H.: Clin. Chem. 19:476, 1973 Beckman Instruments, Inc. Cat. No. 445850	TG or TRIG
Alkaline Phosphatase	AACC Bowers GN, McComb, RB, Clin. Chem. 12:70, 1966 Beckman Instruments, Inc. Cat. No. 442670	ALP or ALK P
Alanine Aminotransferase	Henry Henry RJ, *et al.*: Amer. J. Clin. Path. 34:381, 1960 Beckman Instruments, Inc. Cat. No. 442620	ALT
Aspartate Aminotransferase	Henry Henry RJ, *et al.*: Amer. J. Clin. Path. 34:381, 1960 Beckman Instruments, Inc. Cat. No. 442665	AST
Sodium, Potassium and Chloride	ISE, diluted Cremer, M.: Z. Biologli 47:562, 1906 Stefanac, Z., and Simon W.: Chimica. 20:436-440, 1966 Rosalki, S.B.: J. Lab. Clin. Med. 69:696, 1967 Beckman Instruments, Inc. Cat. No. 443315, 443320, 443325	Na, K, CL
Albumin	Bromcresol green (BCG) Corcoran R, Duran S: Clin. Chem. 23:765-766, 1977 Sigma Diagnostics Cat. No. 631-2	ALBG or ALB
Globulin	Calculated as total protein minus albumin	GLOB
Total Bile Acids	Enzymatic Mashige, F., Tanaka, N., Maki, A., and Kamei, S.: Clin. Chem. 27:1352, 1981 Sigma Diagnostics Cat. No. 450-A	TBA
Sorbitol Dehydrogenase	-β-D(-) Fructose Substrate Asada, M., Galambos J.T.: Gastroenterology 44:578, 1963 Wiesner, I.S., Rawnsley, H.M., Brooks, F.P., Senior, J.R.: Am. J. Dig. Dis. 10:147, 1965 Sigma Diagnostics Cat. No. 50-UV	SDH

Hematology: Baker 9000 Hematology Analyzer. The electronic counting of red blood cells (RBC), white blood cells (WBC), and platelets (PLT or PLAT) is based on the difference in conductivity between blood cells and the diluent in which they are suspended (impedance principle). Measurement of the mean corpuscular volume (MCV) is based on the RBC impedance pulse amplitude. The hemoglobin (HGB) is determined photometrically by the cyanmethemoglobin reaction. The hematocrit (HCT), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) are calculated automatically according to the following formulas:

$HCT = (MCV \times RBC) / 10$ $\quad MCH = (HGB \times 10) / RBC$ $\quad MCHC = HGB \times 100 / HCT$

Nucleated red blood cells (NRBC) are counted as WBC in automated instruments. Therefore, the WBC value is corrected for any NRBC counted:

$$(WBC \times 100) \div (NRBC + 100) = \text{corrected WBC}$$

Differential WBC Count and RBC Morphology: A blood smear is made and stained with Wright-Giemsa stain. Evaluation of the blood film includes identification and counting of a minimum of 100 WBC, examination of RBC for alterations and variation in morphology, and examination of platelets to estimate number and morphologic alterations. The absolute differential WBC value is calculated as follows:

$$\frac{\%\ \text{differential cells} \times WBC / mm^3}{100} = \text{absolute differential cells} / mm^3$$

Parameter	Abbreviation
Nucleated Red Blood Cells	NRBC
Mature Neutrophils	MAT NEU
Lymphocytes	LYMPH
Monocytes	MONO
Eosinophils	EOSIN
Basophils	BASO
Immature Neutrophils	IMM NEU
Packed Cell Volume	PCV

Reticulocytes: Equal volumes of whole blood and New Methylene Blue (0.5%) are incubated in a test tube at room temperature for 15 min. A blood smear is made and the number of reticulocytes is counted per 1000 red blood cells. The absolute value is calculated as follows:

$$\frac{\%\ \text{reticulocytes} \times RBC / mm^3}{100} = \text{retics} / mm^3$$

Acetylcholinesterase Activity Calculations: Acetylcholinesterase method is a photometric test based on the work of Ellman, *et al.*[1] This method is used on the Beckman CX5 automated clinical chemistry analyzer.

Principle: Acetylthiocholine is split into acetate and thiocholine which reacts with dithiobisnitrobenzoic acid (Ellman's reagent) to form the yellow-colored 5-thio-2-nitrobenzoic acid. Increasing color intensity is directly proportional to the acetylcholinesterase activity and is measured kinetically at 410 nm.

Acetylthiocholine + cholinesterases → thiocholine + acetate

Thiocholine + dithiobisnitrobenzoic acid → 5-thio-2-nitrobenzoic acid

I. COLLECTION

A. Blood: Collected into a 1 ml EDTA tube for the rat (orbital sinus).

II. ASSAY

A. Determine the PCV, SOP CP-730R1 (FOR RAT ONLY)

B. Mix EDTA blood

C. Prepare a 1:10 hemolysate (*e.g.*, 50 μl + 450 μl Ellman's with DI H_2O)

D. Centrifuge the remaining blood and remove the plasma

E. Assay both (plasma and hemolysate) for AChE using the CX5 (SOP CP-632R4)

F. Include a tissue blank assay (replace substrate with saline)

G. Use corrected values for calculation of RBC AChE (Substrate U/L - Saline U/L) according to the following:

PCHE = PLASMA AChE
XCHE = PLASMA AChE (blank)
PCHE(C) = PLASMA AChE (CORRECTED) = (PCHE - XCHE)
PCV = HCT
HCHE = HEMOLYSATE AChE
NCHE = HEMOLYSATE AChE (blank)
HCHE(C) = HEMOLYSATE AChE (CORRECTED) X 10 = (HCHE - NCHE) * 10

$$\text{ECHE} = \text{ERYTHROCYTE (RBC) AChE} = \frac{\text{HCHE(C)} - [\text{PCHE(C)} * (1\text{-PCV})]}{\text{PCV}}$$

[1] Ellman, G.L., *et al.*, Biochem. Pharmacol. 7: 88-91 (1961).

Key to Urinalysis Observations Interpretation

Qualitative/Quantitative Analysis

Glucose

0	=	Negative
Trace	=	50 mg/dl
1	=	100 mg/dl
2	=	250 mg/dl
3	=	500 mg/dl
4	=	≥1000 mg/dl

Protein

0	=	Negative
Trace	=	15 mg/dl
1	=	30 mg/dl
2	=	100 mg/dl
3	=	500 mg/dl

Ketones

0	=	Negative
Trace	=	5 mg/dl
1	=	15 mg/dl
2	=	50 mg/dl
3	=	150 mg/dl

Bilirubin

0	=	Negative
1	=	1 mg/dl
2	=	3 mg/dl
3	=	6 mg/dl

Urobilinogen

1	=	1 mg/dl
2	=	4 mg/dl
3	=	8 mg/dl
4	=	12 mg/dl

Miscellaneous

Volume	=	ml
SG	=	g/ml

Blood

0	=	Negative
Trace	=	10/µl
1	=	25/µl
2	=	50/µl
3	=	150/µl
4	=	250/µl

Leukocytes

0	=	Negative
Trace	=	25/µl
1	=	100/µl
2	=	500/µl

Microscopic Analysis

Scale

0	=	None seen
1	=	Occasional noted
2	=	Noted in every field
3	=	Large amounts in every field
4	=	Full fields
HPF	=	High Power Field (400x) or (40x10)
LPF	=	Low Power Field (100x) or (10x10)
Casts	=	number/LPF
EP Cells	=	number/HPF
WBC	=	number/HPF
RBC	=	number/HPF
PO4	=	Scale
MR/NMR	=	Scale
Other	=	Scale
Sperm	=	Scale

Code

MR	=	Motile rods
NMR	=	Nonmotile rods
PO4	=	Phosphate crystals, triple
EP	=	Epithelial cells
RBC	=	Red blood cell(s)
WBC	=	White blood cell(s)
F	=	Fine
GRAN	=	Granular
+	=	Positive
-	=	Negative

Appendix R: Pathology Report

FINAL PATHOLOGY REPORT FOR FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS IITRI PROJECT NUMBER 1052, STUDY NUMBER 3

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SECTION I

PATHOLOGY NARRATIVE

FINAL PATHOLOGY REPORT

FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS IITRI PROJECT NUMBER 1052, STUDY NUMBER 3

INTRODUCTION

This pathology report, submitted by Pathology Associates International (PAI) to IIT Research Institute (IITRI), represents the histopathology findings for the study designated as "Four-Week Dermal Toxicity Study of Tetramethylammonium Hydroxide (TMAH) in Rats," IITRI Project Number 1052, Study Number 3.

The study was conducted to determine the toxicity of the test substance when applied repeatedly to the intact skin of rats.

EXPERIMENTAL DESIGN AND METHODS

Five groups (groups 2-6), each composed of 10 male and 10 female Sprague-Dawley rats, received once daily dermal applications of test article at a constant volume of 1 ml/kg for six hours/day, five days/week for four weeks. The dose levels administered were 0.25, 0.55, 1, 3, and 5% for animals in the low, mid-low, mid, mid-high, and high dose groups, respectively. Also, one group (vehicle control), composed of 10 male and 10 female Sprague-Dawley rats was administered distilled water dermally once daily for six hours/day, five days/week for four weeks. The experimental design is summarized in Table I (Summary of Experimental Design).

All terminal sacrifice animals were anesthetized with sodium pentobarbital and sacrificed by exsanguination. All terminal sacrifice necropsies were performed according to IITRI Standard Operating Procedures and were conducted by PAI personnel. Early death animals were necropsied on the day of death by an approved IITRI technician. Tissues required by the protocol (see Table II, Protocol-Required Tissues) were examined and placed in 10% neutral buffered formalin.

Tissues required for histopathologic evaluation in control (group 1), mid dose (group 4), and mid-high dose (group 5) groups were trimmed and processed to slides in accordance with PAI Standard Operating Procedures. Group 6 (high dose – 5%) animals of both sexes were removed from the study (and not examined histologically) because of significant early mortality. In addition, early death mid-high dose group male 421 and female nos. 434 and 435 had only application sites and gross lesions processed for histopathologic evaluation. These tissues were evaluated by light microscopy and the results were tabulated. Tissues were recorded as "unsuitable/unavailable for complete evaluation" when they were missing in both the original section and in recut and/or retrim attempts to obtain them.

Application sites from low and mid-low dose groups of both sexes were subsequently processed and examined microscopically in order to determine no effect levels.

Treatment-related lesions are summarized in Table III, Summary of Treatment-Related Lesions. Microscopic findings for all groups are summarized in the Project Summary tables (Section II). The mean group severity scores are found in the Severity Summary tables (Section III). Where applicable, all tissue changes received a severity grade based upon the following scale: 1 = minimal, 2 = mild, 3 = moderate, and 4 = marked. The mean group severity was determined by dividing the sum of the severity scores by the number of tissues in the group. Group mean severity grades for application site inflammation were determined by totaling the severity grades for acute, subacute, or chronic active inflammation and dividing by the number of sites examined. This was done in order to compare the relative intensity of all combined inflammation. Microscopic findings in the protocol-required tissues for individual animals are presented in the Tabulated Animal Data tables (Section IV). The correlation of the necropsy findings and histopathology findings are reported in the Correlation of Gross and Microscopic (Micro) Findings (Section V). The codes used as entries in these tables are explained in the Report Codes Table.

The portion of this study performed by PAI was conducted in compliance with the Environmental Protection Agency's Good Laboratory Practice (GLP) Regulations for Nonclinical Laboratory Studies, 40 CFR Part 792.

RESULTS

The Results section is divided into three parts: Necropsy Findings, Diagnostic Terms, and Histopathology Findings. The Necropsy Findings portion describes lesions seen at necropsy or trimming. The Diagnostic Terms portion lists and clarifies diagnostic terminology that may be unclear. Terms listed in the Diagnostic Terms portion of this section include those that are may or may not be test article-related. The Histopathology Findings portion of this section reports the results and provides discussion of the histopathologic evaluation of the tissues.

Necropsy Findings

Gross observations are listed in the correlation of Gross and Microscopic (Micro) Findings report of Section V.

Apparent treatment-related findings included variously described observations of crusts, thickening, and pigmentation/discoloration (brown, pale, red) at the application sites. Most gross observations of crusts were microscopically represented as exudative scabs in association with other observations of necrosis, squamous epithelial hyperplasia, and inflammation.

Red or dark red discoloration of lungs in rats which were found dead generally correlated with moderate diffuse congestion. Other gross necropsy findings in the mid or mid-high dose group rats were either of insufficient incidence or dose group distribution to be considered related to test article administration.

Diagnostic Terms

The morphologic characteristics of observations and lesions, which require comment, are presented in subsequent paragraphs to aid in the interpretation of the data.

Exudative scabs were generally characterized by proteinaceous homogeneously eosinophilic material admixed with effete (often neutrophilic) inflammatory cells and necrotic cellular debris adherent or loosely adherent to the application site surface.

Squamous epithelial hyperplasia consisted of discernibly (often multifocal and/or marginal thickening) increased numbers above a characteristic normal of three to five layers of viable epidermal stratum germanitivum.

Folliculitis was used to differentiate inflammation oriented around hair follicles or adnexal (follicle associated) structures as opposed to unspecified subacute or chronic active inflammation which was found at all levels of the skin. Folliculitis was deemed unrelated to test article administration.

Subacute inflammation generally consisted of a mixed inflammatory cell infiltrate which may have been focally neutrophilic but lacked sufficient fibroplasia to be addressed as chronic active. Sections from various application sites represented a continuum of lesions in both character and intensity of inflammatory cell infiltrate.

Necrosis was used to include areas of coagulation necrosis in which architectural detail was often preserved but the tissue was discernibly not viable.

Eosinophilic intracytoplasmic material was used as a term to further characterize areas of vacuolated hepatocytes (liver) in which apparent intracytoplasmic (often juxtanuclear membrane bound) hepatocellular structures contained homogenous to fibrillar eosinophilic material suggestive of proteinaceous imbibition and/or sequestration to a greater degree than might be occasionally observed in normal control rat livers.

Histopathology Findings

The incidence and average severity of treatment-related histopathology findings are summarized in Table III, Summary of Treatment-Related Lesions. These findings are further discussed in this section of the narrative report.

Application Site

Observations of exudative scab, squamous epithelial hyperplasia, and inflammation (acute, subacute, or chronic active) were observed at all dose levels, including controls, but were discernibly increased in incidence, severity and distribution with increasing dosage applications of test article. Necrosis was a significant component of observations at several application sites, primarily in mid-high (3%) dose groups of both sexes.

Exudative scabs were observed in 2, 0, 0, 3, and 7 of 10 males and 1, 2, 2, 6, and 8 of 10 females in the respective 0, 0.25, 0.55, 1, and 3% dose groups. Squamous epithelial hyperplasia was observed in 1, 1, 1, 6, and 10 of 10 males and 3, 2, 5, 9, and 8 of 10 females in the respective 0, 0.25, 0.55, 1, and 3% dose groups.

Necrosis at the application site was limited to 1 of 10 1% males, 9 of 10 3% males, 1 of 10 0.55% females, 1of 10 1% females, and 8 of 10 3% females.

Inflammation (regardless of acute, subacute or chronic active character) was present in 1, 0, 1, 6, and 10 of 10 males and 2, 5, 5, 8, and 8 of 10 males in the respective 0, 0.25, 0.55, 1, and 3% dose groups.

Additional Findings

Additional findings of thymic lymphoid necrosis (males and females), liver vacuolation (males), liver hepatocellular intracytoplasmic eosinophilic material (males and females), individual hepatocyte necrosis (males), and pulmonary congestion and hemorrhage (males and females) were either limited to mid-high dose rats or distinguishable in incidence from controls at only the 3% mid-high dose level.

Thymic lymphoid necrosis was present in 4 of 9 mid-high dose males and 3 of 8 mid-high dose females. It was of mild severity in two males and of minimal severity in all the other mid-high dose animals.

Pulmonary congestion was generally moderate in severity and confined to the lungs of early death mid-high dose 3% males and females. Five of nine male and four of eight female mid-high dose rats had small foci of hemorrhage in the lungs. One male and two female mid-high dose rats had subtle intra alveolar eosinophilic threads suggestive of fibrin.

Vacuolation was present in the livers of 1 of 10, 0 of 10, and 7 of 9 males in the respective 0, 1, and 3% dose groups. Male mid-high dose liver vacuolation was accompanied by membrane bound homogenous, eosinophilic intracytoplasmic material. The incidence of vacuolation in treated female livers was 6 of 10, 6 of 10, and 3 of 8 in the respective 0, 1, and 3% dose groups. Hepatocellular eosinophilic intracytoplasmic material was limited to two of eight 3% mid-high dose females. Individual hepatocyte necrosis was only present in 3 of 9 3% males. Vacuolation (3% males), eosinophilic intraplasmic material (3% males and females), and individual hepatocyte necrosis (3% males) were considered to be treatment-related.

DISCUSSION

The test article (TMAH) was an apparent direct irritant at the 3% concentration as evidenced by significant necrosis which intermittently extended full thickness through the epidermis and dermis to the level of underlying skeletal muscle. Associated inflammation tended to be limited to the epidermis and dermis with only occasional percolation of inflammatory cells into the underlying skeletal muscle. Inflammation varied in character from acute to focally neutrophilic subacute to chronic active. A few animals had distinct bullous vesicular structures within the epidermis. Squamous epithelial hyperplasia, as a component of the test article administration site effects, was not restricted to marginal areas. In several rats, areas of necrosis included thickened previously hyperplastic epithelium, indicating that in some cases the test article had an initial proliferation effect which gave way to necrosis.

Moderately congested lungs with or without fibrin threads in alveoli may indicate a component of pulmonary compromise in the 3% animals which were found dead.

Thymic lymphoid necrosis in the 3% animals was probably associated with stress.

Inflammation in the salivary glands or associated connective tissue was considered to be a likely sequellae of cervical collars and unrelated to the test article.

In consideration that test article related findings at dosages below 3% were limited to the application site, the establishment of no effect levels was based upon subjective opinion as to the toxicologic significance of incidence and average severity grades of the four lesion components (exudative scab, necrosis, squamous epithelial hyperplasia and inflammation). This interpretation was somewhat obfuscated by the incidences of exudative scab, squamous epithelial hyperplasia and inflammation in control animal application sites.

In this pathologist's opinion, although there was no no-effect level for inflammation in female application sites, the no observable effect levels for the most significant observations of necrosis and squamous epithelial hyperplasia were 0.55% in males and 0.25% in females.

CONCLUSIONS

Daily (six hours per day/five days per week) dermal administration of test article TMAH to rats resulted in observations which were primarily attributed to locally irritative characteristics. The no effect levels for the most significant application site observations of necrosis and squamous epithelial hyperplasia were 0.55% in males and 0.25% in females.

John C. Turnier, VMD
Diplomate, ACVP

May 4, 2000
Date

TABLE I

SUMMARY OF EXPERIMENTAL DESIGN

Group Number	Dose Group	Dose Level (w/w%)	Number of Males	Number of Females
1	Vehicle Control	0	10	10
2	Low	0.25	10	10
3	Mid-Low	0.55	10	10
4	Mid	1	10	10
5	Mid-High	3	10	10
6	High	5	10	10

TABLE II

PROTOCOL-REQUIRED TISSUES

Adrenal glands
Aorta
Bone marrow (sternal)
Brain
Cecum
Colon
Duodenum
Ear tag (ID)
[Epididymides]
Esophagus
[Exorbital lacrimal gland]
[Eyes]
[Femur]
Heart
Ileum
Jejunum
Kidneys
Liver
Lung
Lymph node (submandibular and mesenteric)
[Mammary gland]
Ovaries
Pancreas
Pituitary gland
[Prostate]
Rectum
Salivary gland
Sciatic nerve
[Seminal Vesicle]
[Skeletal muscle]
Skin (application site and untreated)
[Spinal cord (cervical, thoracic, and lumbar)]
Spleen
Stomach
Testes
Thymus
Thyroid/parathyroid
Trachea
Urinary Bladder
Uterus
[Zymbal gland]
Gross Lesions

[ ] = Tissues that were collected but not processed.

TABLE III
SUMMARY OF TREATMENT-RELATED LESIONS

ORGAN - lesion		Dose (w/w%) 0	0.25	0.55	1.0	3.0
SKIN, APPLICATION SITE						
- Exudative scab	M	2/10 (0.40)*	0/10	0/10	3/10 (0.60)	7/10 (1.70)
	F	1/10 (0.20)	2/10 (0.30)	2/10 (0.30)	6/10 (1.30)	8/10 (2.50)
- Necrosis	M	0/10	0/10	0/10	1/10 (0.20)	9/10 (3.00)
	F	0/10	0/10	1/10 (0.20)	1/10 (0.20)	8/10 (2.90)
- Squamous epithelial hyperplasia	M	1/10 (0.20)	1/10 (0.10)	1/10 (0.10)	6/10 (1.10)	10/10 (2.10)
	F	3/10 (0.30)	2/10 (0.40)	5/10 (0.70)	9/10 (1.90)	8/10 (2.10)
- Inflammation (acute, subacute,	M	1/10 (0.20)	0/10	1/10 (0.10)	6/10 (0.70)	10/10 (2.80)
or chronic active)	F	2/10 (0.20)	5/10 (0.50)	6/10 (0.80)	8/10 (1.40)	8/10 (2.60)
THYMUS						
- Lymphoid necrosis	M	0/10	-	-	0/10	4/9 (0.67)
	F	0/10	-	-	0/10	3/8 (0.38)
LIVER						
- Vacuolation	M	1/10 (0.10)	-	-	0/10	7/9 (1.44)
	F	6/10 (0.60)	-	-	6/10 (0.80)	3/8 (0.50)
- Intracytoplasmic eosinophilic	M	0/10	-	-	0/10	7/9 (1.44)
material	F	0/10	-	-	0/10	2/8 (0.25)
- Individual cell necrosis	M	0/10	-	-	0/10	3/9 (0.33)
	F	0/10	-	-	0/10	0/8
LUNGS						
- Congestion	M	0/10	-	-	0/10	7/10 (1.90)
	F	0/10	-	-	0/10	2/8 (0.75)
- Hemorrhage	M	0/10	-	-	2/10 (0.20)	5/10 (0.70)
	F	1/10 (0.20)	-	-	1/10 (0.10)	4/8 (0.50)

* Incidence (mean group severity score)

- Not examined

PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS
IIT RESEARCH INSTITUTE PROJECT NUMBER 1052, STUDY NUMBER 3

Report Codes 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
W	with
Tiss	Tissue

SECTION II

PROJECT SUMMARY

PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
BRAIN	# EX	10		0		0		10		9	
THYMUS	# EX	10		0		0		10		9	
HEMORRHAGE		1	10.0	0	0.0	0	0.0	1	10.0	5	55.6
LYMPHOID NECROSIS		0	0.0	0	0.0	0	0.0	0	0.0	4	44.4
SALIVARY GLAND	# EX	10		0		0		10		9	
INFLAMMATION, SUBACUTE		0	0.0	0	0.0	0	0.0	4	40.0	1	11.1
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS		3	30.0	0	0.0	0	0.0	2	20.0	2	22.2
INFLAMMATION, ACUTE CAPULE/CONNECTIVE TISSUE		1	10.0	0	0.0	0	0.0	0	0.0	1	11.1
INFLAMMATION, CHRONIC ACTIVE CAPSULE/CONN TISS		0	0.0	0	0.0	0	0.0	0	0.0	3	33.3
LYMPH NODE,MANDIBULAR	# EX	10		0		0		10		9	
HEMORRHAGE		3	30.0	0	0.0	0	0.0	1	10.0	3	33.3
REACTIVE HYPERPLASIA		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
PANCREAS	# EX	10		0		0		10		9	
INFLAMMATION, CHRONIC		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
INFLAMMATION, SUBACUTE		0	0.0	0	0.0	0	0.0	1	10.0	0	0.0
SKIN,APPLICATION SITE	# EX	10		10		10		10		10	
EXUDATIVE SCAB		2	20.0	0	0.0	0	0.0	3	30.0	7	70.0
HEMORRHAGE		1	10.0	0	0.0	0	0.0	1	10.0	1	10.0
SQUAMOUS EPITHELIAL HYPERPLASIA		1	10.0	1	10.0	1	10.0	6	60.0	10	100.0
FOLLICULITIS, SUBACUTE		1	10.0	1	10.0	0	0.0	0	0.0	0	0.0
INFLAMMATION, SUBACUTE		1	10.0	0	0.0	1	10.0	4	40.0	5	50.0
INFLAMMATION, CHRONIC ACTIVE		0	0.0	0	0.0	0	0.0	2	20.0	4	40.0
NECROSIS		0	0.0	0	0.0	0	0.0	1	10.0	9	90.0

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/w%)
(2) - (0.25 w/w%)
(3) - (0.55 w/w%)
(4) - (1 w/w%)
(5) - (3 w/w%)

LABCAT HP4.2

31-AUG-1999

PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
SKIN,APPLICATION SITE	# EX	10		10		10		10		10	
INFLAMMATION, ACUTE		0	0.0	0	0.0	0	0.0	0	0.0	1	10.0
VASCULAR THROMBUS		0	0.0	0	0.0	0	0.0	0	0.0	1	10.0
ADRENAL GLAND	# EX	10		0		0		10		9	
ESOPHAGUS	# EX	10		0		0		10		9	
TRACHEA	# EX	10		0		0		10		9	
THYROID GLAND	# EX	10		0		0		10		9	
PARATHYROID GLAND	# EX	10		0		0		10		9	
HEART	# EX	10		0		0		10		9	
INFLAMMATION, SUBACUTE		3	30.0	0	0.0	0	0.0	2	20.0	2	22.2
PROGRESSIVE CARDIOMYOPATHY		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
AORTA	# EX	10		0		0		10		9	
SMALL INTESTINE,DUODENUM	# EX	10		0		0		10		9	
LARGE INTESTINE,COLON	# EX	10		0		0		10		9	
STOMACH	# EX	10		0		0		10		9	
MINERALIZATION, GLANDULAR MUCOSA		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
LIVER	# EX	10		0		0		10		9	
INFLAMMATION, SUBACUTE		7	70.0	0	0.0	0	0.0	8	80.0	7	77.8
MICROGRANULOMA		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
INFLAMMATION, NECROTIZING		0	0.0	0	0.0	0	0.0	2	20.0	0	0.0
INFLAMMATION, CHRONIC CAPSULE		0	0.0	0	0.0	0	0.0	1	10.0	0	0.0
VACUOLATION		1	10.0	0	0.0	0	0.0	0	0.0	7	77.8
EOSINOPHILIC INTRACYTOPLASMIC MATERIAL		0	0.0	0	0.0	0	0.0	0	0.0	7	77.8
AREA OF VACUOLATED/CLEAR CELLS		0	0.0	0	0.0	0	0.0	0	0.0	1	11.1
INDIVIDUAL CELL NECROSIS		0	0.0	0	0.0	0	0.0	0	0.0	3	33.3
SPLEEN	# EX	10		0		0		10		9	
SMALL INTESTINE,JEJUNUM	# EX	10		0		0		10		5	
LUNG	# EX	10		0		0		10		10	
INFLAMMATION, SUBACUTE INTERSTITIAL		1	10.0	0	0.0	0	0.0	0	0.0	1	10.0
ALVEOLAR HISTIOCYTOSIS		1	10.0	0	0.0	0	0.0	2	20.0	1	10.0
PERIVASCULAR NEUTROPHILIC INFILTRATES		2	20.0	0	0.0	0	0.0	4	40.0	4	40.0
HEMORRHAGE		0	0.0	0	0.0	0	0.0	2	20.0	5	50.0
INFLAMMATION, ACUTE INTERSTITIAL		1	10.0	0	0.0	0	0.0	1	10.0	1	10.0
CONGESTION		0	0.0	0	0.0	0	0.0	0	0.0	7	70.0
FIBRIN THREADS WITHIN ALVEOLI		0	0.0	0	0.0	0	0.0	0	0.0	1	10.0
KIDNEY	# EX	10		0		0		10		9	
PYELITIS, SUBACUTE		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA		6	60.0	0	0.0	0	0.0	8	80.0	6	66.7
INFLAMMATION, SUBACUTE		3	30.0	0	0.0	0	0.0	5	50.0	4	44.4
INFLAMMATION, CHRONIC		1	10.0	0	0.0	0	0.0	1	10.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/w%)
(2) - (0.25 w/w%)
(3) - (0.55 w/w%)
(4) - (1 w/w%)
(5) - (3 w/w%)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
KIDNEY	# EX	10		0		0		10		9	
DILATED PELVIS		0	0.0	0	0.0	0	0.0	0	0.0	1	11.1
URINARY BLADDER	# EX	10		0		0		10		9	
LARGE INTESTINE,RECTUM	# EX	10		0		0		10		9	
INFLAMMATION, ACUTE		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
SKIN	# EX	10		0		0		10		9	
INFLAMMATION, SUBACUTE		0	0.0	0	0.0	0	0.0	0	0.0	2	22.2
HYPERKERATOSIS		0	0.0	0	0.0	0	0.0	0	0.0	1	11.1
SMALL INTESTINE,ILEUM	# EX	10		0		0		10		8	
LARGE INTESTINE,CECUM	# EX	10		0		0		10		8	
LYMPH NODE,MESENTERIC	# EX	10		0		0		10		9	
HEMORRHAGE		0	0.0	0	0.0	0	0.0	1	10.0	0	0.0
LYMPHOID NECROSIS		0	0.0	0	0.0	0	0.0	0	0.0	1	11.1
PERIPHERAL NERVE,SCIATIC	# EX	10		0		0		10		9	
TESTES	# EX	10		0		0		10		9	
PITUITARY GLAND	# EX	10		0		0		10		8	
CYST		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/w%)
(2) - (0.25 w/w%)
(3) - (0.55 w/w%)
(4) - (1 w/w%)
(5) - (3 w/w%)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL

SEX: MALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
BONE MARROW,STERNAL	# EX	10		0		0		10		9	

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/w%)
(2) - (0.25 w/w%)
(3) - (0.55 w/w%)
(4) - (1 w/w%)
(5) - (3 w/w%)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
BRAIN	# EX	10		0		0		10		8	
HEMORRHAGE IN VENTRICLE W PIGMENTED MACROPHAGES		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
THYMUS	# EX	10		0		0		10		8	
HEMORRHAGE		3	30.0	0	0.0	0	0.0	1	10.0	4	50.0
LYMPHOID NECROSIS		0	0.0	0	0.0	0	0.0	0	0.0	3	37.5
SALIVARY GLAND	# EX	10		0		0		10		8	
INFLAMMATION, SUBACUTE		1	10.0	0	0.0	0	0.0	1	10.0	0	0.0
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS		3	30.0	0	0.0	0	0.0	6	60.0	3	37.5
HEMMORRHAGE, CONNECTIVE TISSUE		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
LYMPH NODE,MANDIBULAR	# EX	10		0		0		10		8	
HEMORRHAGE		2	20.0	0	0.0	0	0.0	2	20.0	1	12.5
REACTIVE HYPERPLASIA		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
INCREASED FOLLICULAR APOPTOSIS		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
PANCREAS	# EX	10		0		0		10		8	
INFLAMMATION, SUBACUTE		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
SKIN,APPLICATION SITE	# EX	10		10		10		10		10	
EXUDATIVE SCAB		1	10.0	2	20.0	2	20.0	6	60.0	8	80.0
HEMORRHAGE		0	0.0	0	0.0	1	10.0	4	40.0	1	10.0
SQUAMOUS EPITHELIAL HYPERPLASIA		3	30.0	2	20.0	5	50.0	9	90.0	8	80.0
INFLAMMATION, SUBACUTE		0	0.0	4	40.0	3	30.0	3	30.0	3	30.0
INFLAMMATION, CHRONIC ACTIVE		2	20.0	1	10.0	3	30.0	5	50.0	5	50.0
NECROSIS		0	0.0	0	0.0	1	10.0	1	10.0	8	80.0
CONGESTION		0	0.0	0	0.0	0	0.0	0	0.0	1	10.0

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/w%)
(2) - (0.25 w/w%)
(3) - (0.55 w/w%)
(4) - (1 w/w%)
(5) - (3 w/w%)

LABCAT HP4.2 31-AUG-1999

PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
ADRENAL GLAND	# EX	10		0		0		10		8	
DEGENERATION WITH MINERALIZATION		0	0.0	0	0.0	0	0.0	1	10.0	0	0.0
ESOPHAGUS	# EX	10		0		0		10		8	
TRACHEA	# EX	10		0		0		10		8	
HEMORRHAGE		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
THYROID GLAND	# EX	10		0		0		10		8	
PARATHYROID GLAND	# EX	10		0		0		10		7	
HEART	# EX	10		0		0		10		8	
INFLAMMATION, SUBACUTE		4	40.0	0	0.0	0	0.0	2	20.0	1	12.5
CYST, VALVE		0	0.0	0	0.0	0	0.0	1	10.0	0	0.0
AORTA	# EX	10		0		0		10		8	
SMALL INTESTINE,DUODENUM	# EX	10		0		0		10		8	
LARGE INTESTINE,COLON	# EX	10		0		0		10		8	
STOMACH	# EX	10		0		0		10		8	
LIVER	# EX	10		0		0		10		8	
INFLAMMATION, SUBACUTE		10	100.0	0	0.0	0	0.0	8	80.0	4	50.0
VACUOLATION		6	60.0	0	0.0	0	0.0	6	60.0	3	37.5
EOSINOPHILIC INTRACYTOPLASMIC MATERIAL		0	0.0	0	0.0	0	0.0	0	0.0	2	25.0

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

LABCAT HP4.2

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

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INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
SPLEEN	# EX	10		0		0		10		8	
SMALL INTESTINE,JEJUNUM	# EX	10		0		0		10		5	
LUNG	# EX	10		0		0		10		8	
INFLAMMATION, SUBACUTE INTERSTITIAL		0	0.0	0	0.0	0	0.0	1	10.0	1	12.5
ALVEOLAR HISTIOCYTOSIS		3	30.0	0	0.0	0	0.0	4	40.0	2	25.0
PERIVASCULAR NEUTROPHILIC INFILTRATES		5	50.0	0	0.0	0	0.0	5	50.0	6	75.0
HEMORRHAGE		1	10.0	0	0.0	0	0.0	1	10.0	4	50.0
INFLAMMATION, ACUTE INTERSTITIAL		2	20.0	0	0.0	0	0.0	3	30.0	1	12.5
CONGESTION		0	0.0	0	0.0	0	0.0	0	0.0	2	25.0
FIBRIN THREADS WITHIN ALVEOLI		0	0.0	0	0.0	0	0.0	0	0.0	2	25.0
KIDNEY	# EX	10		0		0		10		8	
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA		5	50.0	0	0.0	0	0.0	4	40.0	5	62.5
INFLAMMATION, SUBACUTE		3	30.0	0	0.0	0	0.0	2	20.0	3	37.5
INFLAMMATION, CHRONIC		1	10.0	0	0.0	0	0.0	0	0.0	1	12.5
MINERALIZATION		4	40.0	0	0.0	0	0.0	1	10.0	2	25.0
CYST		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
DILATED TUBULE W PERITUBULAR FIBROSIS		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
URINARY BLADDER	# EX	10		0		0		10		8	
LARGE INTESTINE,RECTUM	# EX	10		0		0		10		8	
INFLAMMATION, ACUTE		2	20.0	0	0.0	0	0.0	0	0.0	0	0.0
SKIN	# EX	10		0		0		10		8	
INFLAMMATION, SUBACUTE		0	0.0	0	0.0	0	0.0	0	0.0	2	25.0

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

PROJECT SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL

SEX: FEMALE

INCIDENCE OF NEOPLASTIC and NON-NEOPLASTIC MICROSCOPIC FINDINGS

GROUP:		VCTL (1)		LOW (2)		MID-LOW (3)		MID (4)		MID-HIGH (5)	
NUMBER OF ANIMALS:		10		10		10		10		10	
		#	%	#	%	#	%	#	%	#	%
SKIN	# EX	10		0		0		10		8	
SQUAMOUS EPITHELIAL HYPERPLASIA		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
FOLLICULITIS, SUBACUTE		0	0.0	0	0.0	0	0.0	1	10.0	0	0.0
SMALL INTESTINE, ILEUM	# EX	10		0		0		10		8	
HEMORRHAGE		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
LARGE INTESTINE, CECUM	# EX	10		0		0		10		8	
LYMPH NODE, MESENTERIC	# EX	10		0		0		10		8	
PERIPHERAL NERVE, SCIATIC	# EX	10		0		0		10		8	
OVARY	# EX	10		0		0		10		8	
CONGESTION		0	0.0	0	0.0	0	0.0	0	0.0	1	12.5
HEMORRHAGE		0	0.0	0	0.0	0	0.0	1	10.0	0	0.0
NORMAL CORPORA LUTEA		1	10.0	0	0.0	0	0.0	0	0.0	0	0.0
UTERUS	# EX	10		0		0		10		8	
PITUITARY GLAND	# EX	10		0		0		10		8	
BONE MARROW, STERNAL	# EX	10		0		0		10		8	

Incidence Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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SECTION III

SEVERITY SUMMARY

PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: MALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
BRAIN	# EX	10	0	0	10	9
THYMUS	# EX	10	0	0	10	9
HEMORRHAGE		1 0.20	0 0.00	0 0.00	1 0.10	5 1.00
LYMPHOID NECROSIS		0 0.00	0 0.00	0 0.00	0 0.00	4 0.67
SALIVARY GLAND	# EX	10	0	0	10	9
INFLAMMATION, SUBACUTE		0 0.00	0 0.00	0 0.00	4 0.60	1 0.33
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS		3 0.30	0 0.00	0 0.00	2 0.50	2 0.33
INFLAMMATION, ACUTE CAPULE/CONNECTIVE TISSUE		1 0.20	0 0.00	0 0.00	0 0.00	1 0.33
INFLAMMATION, CHRONIC ACTIVE CAPSULE/CONN TISS		0 0.00	0 0.00	0 0.00	0 0.00	3 0.56
LYMPH NODE,MANDIBULAR	# EX	10	0	0	10	9
HEMORRHAGE		3 0.50	0 0.00	0 0.00	1 0.10	3 0.44
REACTIVE HYPERPLASIA		1 0.20	0 0.00	0 0.00	0 0.00	0 0.00
PANCREAS	# EX	10	0	0	10	9
INFLAMMATION, CHRONIC		1 0.10	0 0.00	0 0.00	0 0.00	0 0.00
INFLAMMATION, SUBACUTE		0 0.00	0 0.00	0 0.00	1 0.10	0 0.00
SKIN,APPLICATION SITE	# EX	10	10	10	10	10
EXUDATIVE SCAB		2 0.40	0 0.00	0 0.00	3 0.60	7 1.70
HEMORRHAGE		1 0.10	0 0.00	0 0.00	1 0.10	1 0.20
SQUAMOUS EPITHELIAL HYPERPLASIA		1 0.20	1 0.10	1 0.10	6 1.10	10 2.10
FOLLICULITIS, SUBACUTE		1 0.10	1 0.10	0 0.00	0 0.00	0 0.00
INFLAMMATION, SUBACUTE		1 0.20	0 0.00	1 0.10	4 0.40	5 1.30
INFLAMMATION, CHRONIC ACTIVE		0 0.00	0 0.00	0 0.00	2 0.30	4 1.20
NECROSIS		0 0.00	0 0.00	0 0.00	1 0.20	9 3.00
INFLAMMATION, ACUTE		0 0.00	0 0.00	0 0.00	0 0.00	1 0.30

Severity Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: MALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
SKIN,APPLICATION SITE	# EX	10	10	10	10	10
VASCULAR THROMBUS		0 0.00	0 0.00	0 0.00	0 0.00	1 0.20
ADRENAL GLAND	# EX	10	0	0	10	9
ESOPHAGUS	# EX	10	0	0	10	9
TRACHEA	# EX	10	0	0	10	9
THYROID GLAND	# EX	10	0	0	10	9
PARATHYROID GLAND	# EX	10	0	0	10	9
HEART	# EX	10	0	0	10	9
INFLAMMATION, SUBACUTE		3 0.30	0 0.00	0 0.00	2 0.20	2 0.22
PROGRESSIVE CARDIOMYOPATHY		1 0.20	0 0.00	0 0.00	0 0.00	0 0.00
AORTA	# EX	10	0	0	10	9
SMALL INTESTINE,DUODENUM	# EX	10	0	0	10	9
LARGE INTESTINE,COLON	# EX	10	0	0	10	9
STOMACH	# EX	10	0	0	10	9
MINERALIZATION, GLANDULAR MUCOSA		1 0.10	0 0.00	0 0.00	0 0.00	0 0.00
LIVER	# EX	10	0	0	10	9
INFLAMMATION, SUBACUTE		7 0.80	0 0.00	0 0.00	8 0.90	7 0.89
MICROGRANULOMA		1 0.10	0 0.00	0 0.00	0 0.00	0 0.00

Severity Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: MALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
LIVER	# EX	10	0	0	10	9
INFLAMMATION, NECROTIZING		0 0.00	0 0.00	0 0.00	2 0.40	0 0.00
INFLAMMATION, CHRONIC CAPSULE		0 0.00	0 0.00	0 0.00	1 0.20	0 0.00
VACUOLATION		1 0.10	0 0.00	0 0.00	0 0.00	7 1.44
EOSINOPHILIC INTRACYTOPLASMIC MATERIAL		0 0.00	0 0.00	0 0.00	0 0.00	7 1.44
AREA OF VACUOLATED/CLEAR CELLS		0 0.00	0 0.00	0 0.00	0 0.00	1 0.22
INDIVIDUAL CELL NECROSIS		0 0.00	0 0.00	0 0.00	0 0.00	3 0.33
SPLEEN	# EX	10	0	0	10	9
SMALL INTESTINE,JEJUNUM	# EX	10	0	0	10	5
LUNG	# EX	10	0	0	10	10
INFLAMMATION, SUBACUTE INTERSTITIAL		1 0.10	0 0.00	0 0.00	0 0.00	1 0.20
ALVEOLAR HISTIOCYTOSIS		1 0.10	0 0.00	0 0.00	2 0.20	1 0.10
PERIVASCULAR NEUTROPHILIC INFILTRATES		2 0.20	0 0.00	0 0.00	4 0.50	4 0.50
HEMORRHAGE		0 0.00	0 0.00	0 0.00	2 0.20	5 0.70
INFLAMMATION, ACUTE INTERSTITIAL		1 0.20	0 0.00	0 0.00	1 0.10	1 0.10
CONGESTION		0 0.00	0 0.00	0 0.00	0 0.00	7 1.90
FIBRIN THREADS WITHIN ALVEOLI		0 0.00	0 0.00	0 0.00	0 0.00	1 0.10
KIDNEY	# EX	10	0	0	10	9
PYELITIS, SUBACUTE		1 0.30	0 0.00	0 0.00	0 0.00	0 0.00
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA		6 0.60	0 0.00	0 0.00	8 0.80	6 0.78
INFLAMMATION, SUBACUTE		3 0.40	0 0.00	0 0.00	5 0.70	4 0.44
INFLAMMATION, CHRONIC		1 0.10	0 0.00	0 0.00	1 0.20	0 0.00
DILATED PELVIS		0 0.00	0 0.00	0 0.00	0 0.00	1 0.22

Severity Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: MALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
URINARY BLADDER	# EX	10	0	0	10	9
LARGE INTESTINE,RECTUM	# EX	10	0	0	10	9
INFLAMMATION, ACUTE		1 0.10	0 0.00	0 0.00	0 0.00	0 0.00
SKIN	# EX	10	0	0	10	9
INFLAMMATION, SUBACUTE		0 0.00	0 0.00	0 0.00	0 0.00	2 0.33
HYPERKERATOSIS		0 0.00	0 0.00	0 0.00	0 0.00	1 0.11
SMALL INTESTINE,ILEUM	# EX	10	0	0	10	8
LARGE INTESTINE,CECUM	# EX	10	0	0	10	8
LYMPH NODE,MESENTERIC	# EX	10	0	0	10	9
HEMORRHAGE		0 0.00	0 0.00	0 0.00	1 0.10	0 0.00
LYMPHOID NECROSIS		0 0.00	0 0.00	0 0.00	0 0.00	1 0.11
PERIPHERAL NERVE,SCIATIC	# EX	10	0	0	10	9
TESTES	# EX	10	0	0	10	9
PITUITARY GLAND	# EX	10	0	0	10	8
CYST		1 0.20	0 0.00	0 0.00	0 0.00	0 0.00
BONE MARROW,STERNAL	# EX	10	0	0	10	9

Severity Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL
SEX: FEMALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
BRAIN	# EX	10	0	0	10	8
HEMORRHAGE IN VENTRICLE W PIGMENTED MACROPHAGES		1 0.30	0 0.00	0 0.00	0 0.00	0 0.00
THYMUS	# EX	10	0	0	10	8
HEMORRHAGE		3 0.50	0 0.00	0 0.00	1 0.10	4 0.75
LYMPHOID NECROSIS		0 0.00	0 0.00	0 0.00	0 0.00	3 0.38
SALIVARY GLAND	# EX	10	0	0	10	8
INFLAMMATION, SUBACUTE		1 0.20	0 0.00	0 0.00	1 0.10	0 0.00
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS		3 0.50	0 0.00	0 0.00	6 0.60	3 0.62
HEMMORRHAGE, CONNECTIVE TISSUE		0 0.00	0 0.00	0 0.00	0 0.00	1 0.12
LYMPH NODE,MANDIBULAR	# EX	10	0	0	10	8
HEMORRHAGE		2 0.20	0 0.00	0 0.00	2 0.30	1 0.12
REACTIVE HYPERPLASIA		1 0.20	0 0.00	0 0.00	0 0.00	0 0.00
INCREASED FOLLICULAR APOPTOSIS		0 0.00	0 0.00	0 0.00	0 0.00	1 0.25
PANCREAS	# EX	10	0	0	10	8
INFLAMMATION, SUBACUTE		0 0.00	0 0.00	0 0.00	0 0.00	1 0.12
SKIN,APPLICATION SITE	# EX	10	10	10	10	10
EXUDATIVE SCAB		1 0.20	2 0.30	2 0.30	6 1.30	8 2.50
HEMORRHAGE		0 0.00	0 0.00	1 0.20	4 0.40	1 0.10
SQUAMOUS EPITHELIAL HYPERPLASIA		3 0.30	2 0.40	5 0.70	9 1.90	8 2.10
INFLAMMATION, SUBACUTE		0 0.00	4 0.40	3 0.40	3 0.50	3 0.80
INFLAMMATION, CHRONIC ACTIVE		2 0.20	1 0.10	3 0.40	5 0.90	5 1.80
NECROSIS		0 0.00	0 0.00	1 0.20	1 0.20	8 2.90
CONGESTION		0 0.00	0 0.00	0 0.00	0 0.00	1 0.20

Severity Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: FEMALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
ADRENAL GLAND	# EX	10	0	0	10	8
DEGENERATION WITH MINERALIZATION		0 0.00	0 0.00	0 0.00	1 0.30	0 0.00
ESOPHAGUS	# EX	10	0	0	10	8
TRACHEA	# EX	10	0	0	10	8
HEMORRHAGE		0 0.00	0 0.00	0 0.00	0 0.00	1 0.12
THYROID GLAND	# EX	10	0	0	10	8
PARATHYROID GLAND	# EX	10	0	0	10	7
HEART	# EX	10	0	0	10	8
INFLAMMATION, SUBACUTE		4 0.50	0 0.00	0 0.00	2 0.20	1 0.12
CYST, VALVE		0 0.00	0 0.00	0 0.00	1 0.20	0 0.00
AORTA	# EX	10	0	0	10	8
SMALL INTESTINE,DUODENUM	# EX	10	0	0	10	8
LARGE INTESTINE,COLON	# EX	10	0	0	10	8
STOMACH	# EX	10	0	0	10	8
LIVER	# EX	10	0	0	10	8
INFLAMMATION, SUBACUTE		10 1.40	0 0.00	0 0.00	8 1.10	4 0.50
VACUOLATION		6 0.60	0 0.00	0 0.00	6 0.80	3 0.50
EOSINOPHILIC INTRACYTOPLASMIC MATERIAL		0 0.00	0 0.00	0 0.00	0 0.00	2 0.25

Severity Calculated by No. of Tissues Scored
(1) - (0 w/w%)
(2) - (0.25 w/w%)
(3) - (0.55 w/w%)
(4) - (1 w/w%)
(5) - (3 w/w%)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: FEMALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
SPLEEN	# EX	10	0	0	10	8
SMALL INTESTINE,JEJUNUM	# EX	10	0	0	10	5
LUNG	# EX	10	0	0	10	8
INFLAMMATION, SUBACUTE INTERSTITIAL		0 0.00	0 0.00	0 0.00	1 0.10	1 0.12
ALVEOLAR HISTIOCYTOSIS		3 0.30	0 0.00	0 0.00	4 0.40	2 0.25
PERIVASCULAR NEUTROPHILIC INFILTRATES		5 0.90	0 0.00	0 0.00	5 0.70	6 1.00
HEMORRHAGE		1 0.20	0 0.00	0 0.00	1 0.10	4 0.50
INFLAMMATION, ACUTE INTERSTITIAL		2 0.30	0 0.00	0 0.00	3 0.30	1 0.12
CONGESTION		0 0.00	0 0.00	0 0.00	0 0.00	2 0.75
FIBRIN THREADS WITHIN ALVEOLI		0 0.00	0 0.00	0 0.00	0 0.00	2 0.38
KIDNEY	# EX	10	0	0	10	8
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA		5 0.50	0 0.00	0 0.00	4 0.40	5 0.62
INFLAMMATION, SUBACUTE		3 0.40	0 0.00	0 0.00	2 0.30	3 0.50
INFLAMMATION, CHRONIC		1 0.20	0 0.00	0 0.00	0 0.00	1 0.25
MINERALIZATION		4 0.40	0 0.00	0 0.00	1 0.20	2 0.25
CYST		0 0.00	0 0.00	0 0.00	0 0.00	1 0.25
DILATED TUBULE W PERITUBULAR FIBROSIS		0 0.00	0 0.00	0 0.00	0 0.00	1 0.25
URINARY BLADDER	# EX	10	0	0	10	8
LARGE INTESTINE,RECTUM	# EX	10	0	0	10	8
INFLAMMATION, ACUTE		2 0.20	0 0.00	0 0.00	0 0.00	0 0.00
SKIN	# EX	10	0	0	10	8
INFLAMMATION, SUBACUTE		0 0.00	0 0.00	0 0.00	0 0.00	2 0.25
SQUAMOUS EPITHELIAL HYPERPLASIA		0 0.00	0 0.00	0 0.00	0 0.00	1 0.12

Severity Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

SEVERITY SUMMARY

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL
SEX: FEMALE

GROUP:		VCTL (1)	LOW (2)	MID-LOW (3)	MID (4)	MID-HIGH (5)
NUMBER OF ANIMALS:		10	10	10	10	10
		# SEV	# SEV	# SEV	# SEV	# SEV
SKIN	# EX	10	0	0	10	8
FOLLICULITIS, SUBACUTE		0 0.00	0 0.00	0 0.00	1 0.10	0 0.00
SMALL INTESTINE, ILEUM	# EX	10	0	0	10	8
HEMORRHAGE		1 0.10	0 0.00	0 0.00	0 0.00	0 0.00
LARGE INTESTINE, CECUM	# EX	10	0	0	10	8
LYMPH NODE, MESENTERIC	# EX	10	0	0	10	8
PERIPHERAL NERVE, SCIATIC	# EX	10	0	0	10	8
OVARY	# EX	10	0	0	10	8
CONGESTION		0 0.00	0 0.00	0 0.00	0 0.00	1 0.25
HEMORRHAGE		0 0.00	0 0.00	0 0.00	1 0.10	0 0.00
UTERUS	# EX	10	0	0	10	8
PITUITARY GLAND	# EX	10	0	0	10	8
BONE MARROW, STERNAL	# EX	10	0	0	10	8

Severity Calculated by No. of Tissues Scored
(1) - (0 w/wt)
(2) - (0.25 w/wt)
(3) - (0.55 w/wt)
(4) - (1 w/wt)
(5) - (3 w/wt)

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SECTION IV

TABULATED ANIMAL DATA

PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: VCTL: (0 w/w%)
SEX: MALE

ANIMAL ID:	336	337	338	339	340	341	342	343	344	345
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N	N	N		N	N	N	N
HEMORRHAGE	-	-	-	-	-	2	-	-	-	-
SALIVARY GLAND		N			N	N	N	N	N	
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS	1	-	1	1	-	-	-	-	-	-
INFLAMMATION, ACUTE CAPULE/CONNECTIVE TISSUE	-	-	-	-	-	-	-	-	-	2
LYMPH NODE,MANDIBULAR		N	N	N	N			N	N	N
HEMORRHAGE	1	-	-	-	-	2	2	-	-	-
REACTIVE HYPERPLASIA	-	-	-	-	-	2	-	-	-	-
PANCREAS		N	N	N	N	N	N	N	N	N
INFLAMMATION, CHRONIC	1	-	-	-	-	-	-	-	-	-
SKIN,APPLICATION SITE		N	N		N	N	N	N	N	
EXUDATIVE SCAB	2	-	-	-	-	-	-	-	-	2
HEMORRHAGE	1	-	-	-	-	-	-	-	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	2	-	-	-	-	-	-	-	-	-
FOLLICULITIS, SUBACUTE	1	-	-	-	-	-	-	-	-	-
INFLAMMATION, SUBACUTE	-	-	-	2	-	-	-	-	-	-
ADRENAL GLAND	N	N	N	N	N	N	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	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: VCTL: (0 w/w%)
SEX: MALE

ANIMAL ID:	336	337	338	339	340	341	342	343	344	345
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
HEART	N	N		N			N	N	N	
INFLAMMATION, SUBACUTE	-	-	1	-	1	-	-	-	-	1
PROGRESSIVE CARDIOMYOPATHY	-	-	-	-	-	2	-	-	-	-
AORTA	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N		N	N	N	N	N	N
MINERALIZATION, GLANDULAR MUCOSA	-	-	-	1	-	-	-	-	-	-
LIVER		N		N	N					
INFLAMMATION, SUBACUTE	1	-	1	-	-	2	1	1	1	1
MICROGRANULOMA	-	-	-	-	-	-	1	-	-	-
VACUOLATION	-	-	-	-	-	-	-	-	-	1
SPLEEN	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG		N			N	N	N		N	
INFLAMMATION, SUBACUTE INTERSTITIAL	1	-	-	-	-	-	-	-	-	-
ALVEOLAR HISTIOCYTOSIS	-	-	1	-	-	-	-	-	-	-
PERIVASCULAR NEUTROPHILIC INFILTRATES	-	-	-	1	-	-	-	1	-	-
INFLAMMATION, ACUTE INTERSTITIAL	-	-	-	-	-	-	-	-	-	2
KIDNEY		N		N						
PYELITIS, SUBACUTE	3I	-	-	-	-	-	-	-	-	-

See Reports Code Table for Symbol Definitions

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL GROUP: VCTL: (0 w/wt)
SEX: MALE

ANIMAL ID:	336	337	338	339	340	341	342	343	344	345
KIDNEY		N		N						
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA	1I	-	1L	-	-	1I	1L	1L	-	1L
INFLAMMATION, SUBACUTE	-	-	-	-	1L	2L	1L	-	-	-
INFLAMMATION, CHRONIC	-	-	-	-	-	-	-	-	1L	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,RECTUM		N	N	N	N	N	N	N	N	N
INFLAMMATION, ACUTE	1	-	-	-	-	-	-	-	-	-
SKIN	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,CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	N	N	N	N
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	
CYST	-	-	-	-	-	-	-	-	-	2
BONE MARROW,STERNAL	N	N	N	N	N	N	N	N	N	N

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL GROUP: LOW: (0.25 w/w%)
SEX: MALE

ANIMAL ID:	356	357	358	359	360	361	362	363	364	365
SKIN,APPLICATION SITE	N	N	N	N	N	N		N	N	
SQUAMOUS EPITHELIAL HYPERPLASIA	-	-	-	-	-	-	1	-	-	-
FOLLICULITIS, SUBACUTE	-	-	-	-	-	-	-	-	-	1

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL GROUP: MID-LOW: (0.55 w/w%)
SEX: MALE

ANIMAL ID:	376	377	378	379	380	381	382	383	384	385
SKIN,APPLICATION SITE	M	M		M	M	M	M		M	M
SQUAMOUS EPITHELIAL HYPERPLASIA	-	-	1	-	-	-	-	-	-	-
INFLAMMATION, SUBACUTE	-	-	-	-	-	-	-	1	-	-

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: MID: (1 w/w%)
SEX: MALE

ANIMAL ID:	396	397	398	399	400	401	402	403	404	405
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS	N	N	N		N	N	N	N	N	N
HEMORRHAGE	-	-	-	1	-	-	-	-	-	-
SALIVARY GLAND	N	N			N	N		N		N
INFLAMMATION, SUBACUTE	-	-	2	1	-	-	1	-	2	-
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS	-	-	2	-	-	-	-	-	3	-
LYMPH NODE,MANDIBULAR	N		N	N	N	N	N	N	N	N
HEMORRHAGE	-	1	-	-	-	-	-	-	-	-
PANCREAS	N	N	N	N	N	N	N	N		N
INFLAMMATION, SUBACUTE	-	-	-	-	-	-	-	-	1	-
SKIN,APPLICATION SITE	N			N			N			
EXUDATIVE SCAB	-	-	3	-	1	-	-	2	-	-
HEMORRHAGE	-	-	-	-	-	-	-	1	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	-	1	3	-	2	2	-	2	1	-
INFLAMMATION, SUBACUTE	-	-	-	-	1	-	-	1	1	1
INFLAMMATION, CHRONIC ACTIVE	-	-	2	-	-	1	-	-	-	-
NECROSIS	-	-	-	-	2	-	-	-	-	-
ADRENAL GLAND	N	N	N	N	N	N	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	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: MID: (1 w/wt)
SEX: MALE

ANIMAL ID:	396	397	398	399	400	401	402	403	404	405
HEART	N	N	N	N	N		N	N	N	
INFLAMMATION, SUBACUTE	-	-	-	-	-	1	-	-	-	1
AORTA	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER			N					N		
INFLAMMATION, SUBACUTE	2	1	-	1	1	1	1	-	1	1
INFLAMMATION, NECROTIZING	-	2	-	-	-	2	-	-	-	-
INFLAMMATION, CHRONIC CAPSULE	-	-	-	-	-	2	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG					N	N			N	
ALVEOLAR HISTIOCYTOSIS	-	-	1	1	-	-	-	-	-	-
PERIVASCULAR NEUTROPHILIC INFILTRATES	1	-	-	1	-	-	-	2	-	1
HEMORRHAGE	1	1	-	-	-	-	-	-	-	-
INFLAMMATION, ACUTE INTERSTITIAL	-	-	-	-	-	-	1	-	-	-
KIDNEY										
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA	1L	1L	1I	1I	1L	-	1L	1I	1L	-
INFLAMMATION, SUBACUTE	-	3I	-	-	-	1L	-	1L	1L	1L
INFLAMMATION, CHRONIC	-	-	-	-	-	-	-	-	-	2L
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: MID: (1 w/w%)
SEX: MALE

ANIMAL ID:	396	397	398	399	400	401	402	403	404	405
LARGE INTESTINE,RECTUM	N	N	N	N	N	N	N	N	N	N
SKIN	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,CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N		N	N	N	N	N	N	N
HEMORRHAGE	-	-	1	-	-	-	-	-	-	-
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	N
TESTES	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
BONE MARROW,STERNAL	N	N	N	N	N	N	N	N	N	N

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: MID-HIGH: (3 w/w%)
SEX: MALE

ANIMAL ID:	416	417	418	419	420	421	422	423	424	425
BRAIN	N	N	N	N	N		N	N	N	N
THYMUS								N		N
HEMORRHAGE	2	2	1	-	2	-	2	-	-	-
LYMPHOID NECROSIS	-	-	-	1	2	-	2	-	1	-
SALIVARY GLAND	N	N								N
INFLAMMATION, SUBACUTE	-	-	-	-	-	-	-	3	-	-
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS	-	-	-	-	-	-	-	2	1	-
INFLAMMATION, ACUTE CAPULE/CONNECTIVE TISSUE	-	-	-	-	3	-	-	-	-	-
INFLAMMATION, CHRONIC ACTIVE CAPSULE/CONN TISS	-	-	2	2	-	-	1	-	-	-
LYMPH NODE,MANDIBULAR		N	N	N			N	N		N
HEMORRHAGE	1	-	-	-	2	-	-	-	1	-
PANCREAS	N	N	N	N	N		N	N	N	N
SKIN,APPLICATION SITE										
EXUDATIVE SCAB	2	3	3	3	-	-	-	3	1	2
HEMORRHAGE	-	-	-	-	-	2	-	-	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	2	2	3	2	2	2	1	3	2	2
INFLAMMATION, SUBACUTE	2	3	3	2	3	-	-	-	-	-
INFLAMMATION, CHRONIC ACTIVE	-	-	-	-	-	-	3	3	3	3
NECROSIS	-	3	4	2	3	4	4	3	4	3
INFLAMMATION, ACUTE	-	-	-	-	-	3	-	-	-	-
VASCULAR THROMBUS	-	-	-	-	-	2	-	-	-	-
ADRENAL GLAND	N	N	N	N	N		N	N	N	N
ESOPHAGUS	N	N	N	N	N		N	N	N	N
TRACHEA	N	N	N	N	N		N	N	N	N

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: MID-HIGH: (3 w/w%)
SEX: MALE

ANIMAL ID:	416	417	418	419	420	421	422	423	424	425
THYROID GLAND	N	N	N	N	N		N	N	N	N
PARATHYROID GLAND	N	N	N	N	N		N	N	N	N
HEART	N	N		N	N		N	N	N	
INFLAMMATION, SUBACUTE	-	-	1	-	-	-	-	-	-	1
AORTA	N	N	N	N	N		N	N	N	N
SMALL INTESTINE,DUODENUM	N	N	N	N	N		N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N		N	N	N	N
STOMACH	N	N	N	N	N		N	N	N	N
LIVER										
INFLAMMATION, SUBACUTE	-	1	1	1	1	-	1	2	-	1
VACUOLATION	2	1	2	2	2	-	2	-	2	-
EOSINOPHILIC INTRACYTOPLASMIC MATERIAL	2	1	2	2	2	-	2	-	2	-
AREA OF VACUOLATED/CLEAR CELLS	-	-	-	-	-	-	-	2	-	-
INDIVIDUAL CELL NECROSIS	1	-	-	1	1	-	-	-	-	-
SPLEEN	N	N	N	N	N		N	N	N	N
SMALL INTESTINE,JEJUNUM	A	N	A	N	A		N	N	A	N
LUNG										N
INFLAMMATION, SUBACUTE INTERSTITIAL	-	-	-	-	-	-	2	-	-	-
ALVEOLAR HISTIOCYTOSIS	-	-	-	-	-	-	-	1	-	-
PERIVASCULAR NEUTROPHILIC INFILTRATES	-	-	1	-	-	1	-	2	1	-
HEMORRHAGE	-	1	2	2	-	-	-	1	1	-
INFLAMMATION, ACUTE INTERSTITIAL	-	-	-	1	-	-	-	-	-	-

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: MID-HIGH: (3 w/w%)
SEX: MALE

ANIMAL ID:	416	417	418	419	420	421	422	423	424	425
LUNG										N
CONGESTION	3	-	3	1	3	3	3	-	3	-
FIBRIN THREADS WITHIN ALVEOLI	-	-	-	-	1	-	-	-	-	-
KIDNEY					N					
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA	1L	2L	1L	-	-	-	1L	-	1L	1L
INFLAMMATION, SUBACUTE	-	-	-	1L	-	-	-	1L	1L	1L
DILATED PELVIS	-	-	-	-	-	-	2L	-	-	-
URINARY BLADDER	N	N	N	N	N		N	N	N	N
LARGE INTESTINE,RECTUM	N	N	N	N	N		N	N	N	N
SKIN	N		N				N	N	N	N
INFLAMMATION, SUBACUTE	-	1	-	-	2	-	-	-	-	-
HYPERKERATOSIS	-	-	-	1	-	-	-	-	-	-
SMALL INTESTINE,ILEUM	N	N	N	N	A		N	N	N	N
LARGE INTESTINE,CECUM	N	N	N	N	A		N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N		N		N	N	N	N
LYMPHOID NECROSIS	-	-	-	1	-	-	-	-	-	-
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N		N	N	N	N
TESTES	N	N	N	N	N		N	N	N	N
PITUITARY GLAND	U	N	N	N	N		N	N	N	N
BONE MARROW,STERNAL	N	N	N	N	N		N	N	N	N

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: VCTL: (0 w/w%)
SEX: FEMALE

ANIMAL ID:	346	347	348	349	350	351	352	353	354	355
BRAIN		N	N	N	N	N	N	N	N	N
HEMORRHAGE IN VENTRICLE W PIGMENTED MACROPHAGES	3	-	-	-	-	-	-	-	-	-
THYMUS	N	N		N	N		N	N	N	
HEMORRHAGE	-	-	1	-	-	2	-	-	-	2
SALIVARY GLAND		N	N		N	N	N	N		N
INFLAMMATION, SUBACUTE	2	-	-	-	-	-	-	-	-	-
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS	2	-	-	1	-	-	-	-	2	-
LYMPH NODE,MANDIBULAR	N	N			N	N	N	N	N	
HEMORRHAGE	-	-	1	-	-	-	-	-	-	1
REACTIVE HYPERPLASIA	-	-	-	2	-	-	-	-	-	-
PANCREAS	N	N	N	N	N	N	N	N	N	N
SKIN,APPLICATION SITE		N		N	N	N			N	N
EXUDATIVE SCAB	-	-	-	-	-	-	-	2	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	1	-	-	-	-	-	1	1	-	-
INFLAMMATION, CHRONIC ACTIVE	-	-	1	-	-	-	1	-	-	-
ADRENAL GLAND	N	N	N	N	N	N	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	N
THYROID GLAND	N	N	N	N	N	N	N	N	N	N
PARATHYROID GLAND	N	N	N	N	N	N	N	N	N	N
HEART	N	N				N	N	N		N

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: VCTL: (0 w/w%)
SEX: FEMALE

ANIMAL ID:	346	347	348	349	350	351	352	353	354	355
HEART	N	N				N	N	N		N
INFLAMMATION, SUBACUTE	-	-	2	1	1	-	-	-	1	-
AORTA	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER										
INFLAMMATION, SUBACUTE	1	2	2	1	1	1	1	1	2	2
VACUOLATION	1	-	1	1	1	-	-	1	1	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG				N				N		
ALVEOLAR HISTIOCYTOSIS	-	-	-	-	-	1	-	-	1	1
PERIVASCULAR NEUTROPHILIC INFILTRATES	2	2	1	-	2	-	2	-	-	-
HEMORRHAGE	-	-	-	-	-	-	-	-	-	2
INFLAMMATION, ACUTE INTERSTITIAL	1	-	-	-	-	-	-	-	-	2
KIDNEY			N					N	N	N
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA	-	1L	-	1L	1L	1L	1L	-	-	-
INFLAMMATION, SUBACUTE	-	-	-	1L	2L	-	1L	-	-	-
INFLAMMATION, CHRONIC	2L	-	-	-	-	-	-	-	-	-
MINERALIZATION	-	-	-	1I	1I	1L	1L	-	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: VCTL: (0 w/w%)
SEX: FEMALE

ANIMAL ID:	346	347	348	349	350	351	352	353	354	355
LARGE INTESTINE,RECTUM	N	N	N		N	N		N	N	N
INFLAMMATION, ACUTE	-	-	-	1	-	-	1	-	-	-
SKIN	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,ILEUM	N	N	N	N		N	N	N	N	N
HEMORRHAGE	-	-	-	-	1	-	-	-	-	-
LARGE INTESTINE,CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	N	N	N	N
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N	N	N		N	N
NORMAL CORPORA LUTEA	-	-	-	-	-	-	-	P	-	-
UTERUS	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
BONE MARROW,STERNAL	N	N	N	N	N	N	N	N	N	N

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PATHOLOGY ASSOCIATES INTERNATIONAL
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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: LOW: (0.25 w/w%)
SEX: FEMALE

ANIMAL ID:	366	367	368	369	370	371	372	373	374	375
SKIN,APPLICATION SITE					N	N	N	N	N	
EXUDATIVE SCAB	-	-	2	1	-	-	-	-	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	-	-	2	2	-	-	-	-	-	-
INFLAMMATION, SUBACUTE	1	1	1	1	-	-	-	-	-	-
INFLAMMATION, CHRONIC ACTIVE	-	-	-	-	-	-	-	-	-	1

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 STUDY NUMBER: 1052SN3
FATE: ALL GROUP: MID-LOW: (0.55 w/w%)
SEX: FEMALE

ANIMAL ID:	386	387	388	389	390	391	392	393	394	395
SKIN,APPLICATION SITE	N	N							N	
EXUDATIVE SCAB	-	-	-	-	-	-	2	-	-	1
HEMORRHAGE	-	-	-	-	-	-	2	-	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	-	-	-	1	2	-	2	1	-	1
INFLAMMATION, SUBACUTE	-	-	-	-	-	1	2	1	-	-
INFLAMMATION, CHRONIC ACTIVE	-	-	1	-	2	-	-	-	-	1
NECROSIS	-	-	-	-	-	-	2	-	-	-

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: MID: (1 w/w%)
SEX: FEMALE

ANIMAL ID:	406	407	408	409	410	411	412	413	414	415
BRAIN	N	N	N	N	N	N	N	N	N	N
THYMUS	N		N	N	N	N	N	N	N	N
HEMORRHAGE	-	1	-	-	-	-	-	-	-	-
SALIVARY GLAND	N	N		N		N				
INFLAMMATION, SUBACUTE	-	-	-	-	-	-	-	-	-	1
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS	-	-	1	-	1	-	1	1	1	1
LYMPH NODE,MANDIBULAR		N	N	N	N	N	N	N	N	
HEMORRHAGE	1	-	-	-	-	-	-	-	-	2
PANCREAS	N	N	N	N	N	N	N	N	N	N
SKIN,APPLICATION SITE										N
EXUDATIVE SCAB	3	-	2	2	3	1	-	-	2	-
HEMORRHAGE	1	-	-	1	1	-	-	-	1	-
SQUAMOUS EPITHELIAL HYPERPLASIA	3	2	2	2	3	2	2	1	2	-
INFLAMMATION, SUBACUTE	2	-	-	-	-	1	-	-	2	-
INFLAMMATION, CHRONIC ACTIVE	-	2	1	2	2	-	2	-	-	-
NECROSIS	-	-	-	-	-	-	-	-	2	-
ADRENAL GLAND	N	N	N	N	N	N	N	N	N	
DEGENERATION WITH MINERALIZATION	-	-	-	-	-	-	-	-	-	3L
ESOPHAGUS	N	N	N	N	N	N	N	N	N	N
TRACHEA	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	N	N	N

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3 — STUDY NUMBER: 1052SN3
FATE: ALL — GROUP: MID: (1 w/w%)
SEX: FEMALE

ANIMAL ID:	406	407	408	409	410	411	412	413	414	415
HEART	N	N		N	N		N	N	N	
INFLAMMATION, SUBACUTE	-	-	1	-	-	1	-	-	-	-
CYST, VALVE	-	-	-	-	-	-	-	-	-	2
AORTA	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N	N	N
STOMACH	N	N	N	N	N	N	N	N	N	N
LIVER				N						N
INFLAMMATION, SUBACUTE	3	1	1	-	1	2	1	1	1	-
VACUOLATION	1	1	2	-	2	-	-	1	1	-
SPLEEN	N	N	N	N	N	N	N	N	N	N
SMALL INTESTINE,JEJUNUM	N	N	N	N	N	N	N	N	N	N
LUNG	N						N	N		
INFLAMMATION, SUBACUTE INTERSTITIAL	-	-	-	-	-	-	-	-	-	1
ALVEOLAR HISTIOCYTOSIS	-	-	1	-	1	1	-	-	-	1
PERIVASCULAR NEUTROPHILIC INFILTRATES	-	1	1	2	1	-	-	-	2	-
HEMORRHAGE	-	1	-	-	-	-	-	-	-	-
INFLAMMATION, ACUTE INTERSTITIAL	-	1	1	1	-	-	-	-	-	-
KIDNEY	N	N		N	N					
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA	-	-	1L	-	-	1I	-	1L	-	1L
INFLAMMATION, SUBACUTE	-	-	-	-	-	-	1L	-	2L	-
MINERALIZATION	-	-	-	-	-	2I	-	-	-	-

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: MID: (1 w/w%)
SEX: FEMALE

ANIMAL ID:	406	407	408	409	410	411	412	413	414	415
URINARY BLADDER	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,RECTUM	N	N	N	N	N	N	N	N	N	N
SKIN	N	N	N	N	N		N	N	N	N
FOLLICULITIS, SUBACUTE	-	-	-	-	-	1	-	-	-	-
SMALL INTESTINE,ILEUM	N	N	N	N	N	N	N	N	N	N
LARGE INTESTINE,CECUM	N	N	N	N	N	N	N	N	N	N
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	N	N	N	N
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N	N	N
OVARY	N	N	N	N	N		N	N	N	N
HEMORRHAGE	-	-	-	-	-	1L	-	-	-	-
UTERUS	N	N	N	N	N	N	N	N	N	N
PITUITARY GLAND	N	N	N	N	N	N	N	N	N	N
BONE MARROW,STERNAL	N	N	N	N	N	N	N	N	N	N

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: MID-HIGH: (3 w/w%)
SEX: FEMALE

ANIMAL ID:	426	427	428	429	430	431	432	433	434	435
BRAIN	N	N	N	N	N	N	N	N		
THYMUS	N						N			
HEMORRHAGE	-	2	-	-	2	1	-	1	-	-
LYMPHOID NECROSIS	-	-	1	1	-	1	-	-	-	-
SALIVARY GLAND	N	N	N			N	N			
INFLAMMATION, SUBACUTE CAPSULE/CONNECTIVE TISS	-	-	-	1	2	-	-	2	-	-
HEMMORRHAGE, CONNECTIVE TISSUE	-	-	-	-	-	-	-	1	-	-
LYMPH NODE,MANDIBULAR		N	N	N	N		N	N		
HEMORRHAGE	1	-	-	-	-	-	-	-	-	-
INCREASED FOLLICULAR APOPTOSIS	-	-	-	-	-	2	-	-	-	-
PANCREAS		N	N	N	N	N	N	N		
INFLAMMATION, SUBACUTE	1	-	-	-	-	-	-	-	-	-
SKIN,APPLICATION SITE										
EXUDATIVE SCAB	3	4	3	3	3	4	3	2	-	-
HEMORRHAGE	1	-	-	-	-	-	-	-	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	3	2	3	2	3	3	3	2	-	-
INFLAMMATION, SUBACUTE	-	2	-	3	-	-	-	3	-	-
INFLAMMATION, CHRONIC ACTIVE	3	-	3	-	4	4	4	-	-	-
NECROSIS	-	4	3	4	4	4	-	4	3	3
CONGESTION	-	-	-	-	-	-	-	2	-	-
ADRENAL GLAND	N	N	N	N	N	N	N	N		
ESOPHAGUS	N	N	N	N	N	N	N	N		
TRACHEA	N	N	N		N	N	N	N		
HEMORRHAGE	-	-	-	1	-	-	-	-	-	-

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: MID-HIGH: (3 w/w%)
SEX: FEMALE

ANIMAL ID:	426	427	428	429	430	431	432	433	434	435
THYROID GLAND	N	N	N	N	N	N	N	N		
PARATHYROID GLAND	N	N	U	N	N	N	N	N		
HEART		N	N	N	N	N	N	N		
INFLAMMATION, SUBACUTE	1	-	-	-	-	-	-	-	-	-
AORTA	N	N	N	N	N	N	N	N		
SMALL INTESTINE,DUODENUM	N	N	N	N	N	N	N	N		
LARGE INTESTINE,COLON	N	N	N	N	N	N	N	N		
STOMACH	N	N	N	N	N	N	N	N		
LIVER										
INFLAMMATION, SUBACUTE	-	-	-	1	1	-	1	1	-	-
VACUOLATION	2	1	-	-	-	1	-	-	-	-
EOSINOPHILIC INTRACYTOPLASMIC MATERIAL	-	1	1	-	-	-	-	-	-	-
SPLEEN	N	N	N	N	N	N	N	N		
SMALL INTESTINE,JEJUNUM	N	N	N	A	A	A	N	N		
LUNG										
INFLAMMATION, SUBACUTE INTERSTITIAL	-	-	-	-	1	-	-	-	-	-
ALVEOLAR HISTIOCYTOSIS	1	-	-	-	-	-	1	-	-	-
PERIVASCULAR NEUTROPHILIC INFILTRATES	1	1	1	2	1	2	-	-	-	-
HEMORRHAGE	-	1	1	1	-	-	-	1	-	-
INFLAMMATION, ACUTE INTERSTITIAL	-	-	-	-	-	-	-	1	-	-
CONGESTION	-	3	3	-	-	-	-	-	-	-
FIBRIN THREADS WITHIN ALVEOLI	-	2	-	1	-	-	-	-	-	-

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

TABULATED ANIMAL DATA

STUDY ID : 1052 SN3
FATE: ALL

STUDY NUMBER: 1052SN3
GROUP: MID-HIGH: (3 w/w%)
SEX: FEMALE

ANIMAL ID:	426	427	428	429	430	431	432	433	434	435
KIDNEY								N		
TUBULAR EPITHELIAL BASOPHILIA/HYPERPLASIA	-	1L	1L	1L	1I	1L	-	-	-	-
INFLAMMATION, SUBACUTE	-	2L	1L	-	-	-	1L	-	-	-
INFLAMMATION, CHRONIC	-	2L	-	-	-	-	-	-	-	-
MINERALIZATION	-	1I	-	-	-	1L	-	-	-	-
CYST	-	2L	-	-	-	-	-	-	-	-
DILATED TUBULE W PERITUBULAR FIBROSIS	2L	-	-	-	-	-	-	-	-	-
URINARY BLADDER	N	N	N	N	N	N	N	N		
LARGE INTESTINE,RECTUM	N	N	N	N	N	N	N	N		
SKIN	N			N	N	N	N	N		
INFLAMMATION, SUBACUTE	-	1	1	-	-	-	-	-	-	-
SQUAMOUS EPITHELIAL HYPERPLASIA	-	1	-	-	-	-	-	-	-	-
SMALL INTESTINE,ILEUM	N	N	N	N	N	N	N	N		
LARGE INTESTINE,CECUM	N	N	N	N	N	N	N	N		
LYMPH NODE,MESENTERIC	N	N	N	N	N	N	N	N		
PERIPHERAL NERVE,SCIATIC	N	N	N	N	N	N	N	N		
OVARY	N	N	N	N		N	N	N		
CONGESTION	-	-	-	-	2I	-	-	-	-	-
UTERUS	N	N	N	N	N	N	N	N		
PITUITARY GLAND	N	N	N	N	N	N	N	N		
BONE MARROW,STERNAL	N	N	N	N	N	N	N	N		

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SECTION V

CORRELATION OF GROSS AND MICROSCOPIC (MICRO) FINDINGS

PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3
SEX: MALE

STUDY NUMBER: 1052SN3
GROUP: VCTL: (0 w/wt)

Animal ID: 336
Animal Fate: Terminal sacrifice

Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 3X3 MM	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 341
Animal Fate: Terminal sacrifice

Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
LYMPH NODE,MANDIBULAR - ENLARGED, RED	LYMPH NODE,MANDIBULAR - HEMORRHAGE; REACTIVE HYPERPLASIA
THYMUS - PIGMENTATION, RED	THYMUS - HEMORRHAGE

Animal ID: 345
Animal Fate: Terminal sacrifice

Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 1X2 MM, MULTIPLE	SKIN,APPLICATION SITE - EXUDATIVE SCAB

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3
SEX: MALE

STUDY NUMBER: 1052SN3
GROUP: LOW: (0.25 w/wt)

No Gross Observations for any animal in this group

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 STUDY NUMBER: 1052SN3
SEX: MALE GROUP: MID-LOW: (0.55 w/wt)

Animal ID: 378
Animal Fate: Terminal sacrifice Days on Test: 29

Reference to Necropsy Record:
SKIN,APPLICATION SITE - CRUST, 3X3 MM

Related Histopathology:
SKIN,APPLICATION SITE - NO CORRESPONDING LESION

Animal ID: 379
Animal Fate: Terminal sacrifice Days on Test: 29

Reference to Necropsy Record:
SKIN - FACE, CRUST, (AROUND EYES)

Related Histopathology:
SKIN - FACE, NOT REQUIRED BY PROTOCOL

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: MALE — GROUP: MID: (1 w/w%)

Animal ID: 398
Animal Fate: Terminal sacrifice — Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 3X2 MM	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 400
Animal Fate: Terminal sacrifice — Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 2X2 MM, MULTIPLE	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 403
Animal Fate: Terminal sacrifice — Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 3X4 MM, (M8)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: MALE — GROUP: MID-HIGH: (3 w/w%)

Animal ID: 416
Animal Fate: Natural death — Days on Test: 9

Reference to Necropsy Record:	Related Histopathology:
LUNG - PARENCHYMA, PIGMENTATION, RED	LUNG - CONGESTION
SKIN,APPLICATION SITE - LESION, (SCALY)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 417
Animal Fate: Natural death — Days on Test: 9

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - LESION, (SCALY)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 418
Animal Fate: Natural death — Days on Test: 9

Reference to Necropsy Record:	Related Histopathology:
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - CONGESTION
SKIN,APPLICATION SITE - LESION, (SCAB)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 419
Animal Fate: Natural death — Days on Test: 8

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, PALE	SKIN,APPLICATION SITE - NECROSIS
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - HEMORRHAGE

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: MALE — GROUP: MID-HIGH: (3 w/w%)

Animal ID: 420
Animal Fate: Natural death — Days on Test: 4

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, PALE	SKIN,APPLICATION SITE - NECROSIS
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - CONGESTION
URINARY BLADDER - LUMEN, CALCULUS, WHITE	URINARY BLADDER - NO CORRESPONDING LESION

Animal ID: 421
Animal Fate: Natural death — Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - HEMORRHAGE
LUNG - PARENCHYMA, PIGMENTATION, DARK	LUNG - CONGESTION

Animal ID: 422
Animal Fate: Natural death — Days on Test: 3

Reference to Necropsy Record:	Related Histopathology:
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - CONGESTION
CAVITIES - CRANIAL, RED, (POSSIBLE BLOOD)	CAVITIES - NO SECTION TAKEN
KIDNEY - RIGHT, LESION, (HYDRONEPHROSIS)	KIDNEY - DILATED PELVIS
LIVER - CAUDATE LOBE, FOCUS, 3X3 MM, TAN	LIVER - NO CORRESPONDING LESION

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: MALE — GROUP: MID-HIGH: (3 w/wt)

Animal ID: 423
Animal Fate: Terminal sacrifice — Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 5X2 MM, MULTIPLE, RED	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 424
Animal Fate: Natural death — Days on Test: 9

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, PALE	SKIN,APPLICATION SITE - NECROSIS
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - CONGESTION

Animal ID: 425
Animal Fate: Terminal sacrifice — Days on Test: 29

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 20X20 MM, MULTIPLE, (M8)	SKIN,APPLICATION SITE - EXUDATIVE SCAB
SKIN,APPLICATION SITE - CRUST, 10X10 MM, MULTIPLE, (R8)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: MALE — GROUP: HIGH: (5 w/wt)

Animal ID: 436
Animal Fate: Natural death — Days on Test: 3

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, RED	LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 437
Animal Fate: Natural death — Days on Test: 3

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK, GREY	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, RED	LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 438
Animal Fate: Natural death — Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3
STUDY NUMBER: 1052SN3
SEX: MALE
GROUP: HIGH: (5 w/wt)

Animal ID: 439
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, RED	LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 440
Animal Fate: Natural death
Days on Test: 3

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

Animal ID: 441
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

Animal ID: 442
Animal Fate: Natural death
Days on Test: 1

Reference to Necropsy Record:	Related Histopathology:
SKIN - DORSAL, PIGMENTATION, WHITE, (SKIN AT TEST SITE BLANCHED)	SKIN - NOT REQUIRED BY PROTOCOL

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: MALE — GROUP: HIGH: (5 w/wt)

Animal ID: 443
Animal Fate: Natural death — Days on Test: 3

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, RED	LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 444
Animal Fate: Natural death — Days on Test: 1

Reference to Necropsy Record:	Related Histopathology:
SKIN - DORSAL, PIGMENTATION, WHITE, (SKIN AT TEST SITE BLANCHED)	SKIN - NOT REQUIRED BY PROTOCOL

Animal ID: 445
Animal Fate: Natural death — Days on Test: 8

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - LESION, 15X9 MM	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: FEMALE — GROUP: VCTL: (0 w/w%)

Animal ID: 349
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
LYMPH NODE,MANDIBULAR - ENLARGED	LYMPH NODE,MANDIBULAR - REACTIVE HYPERPLASIA

Animal ID: 351
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, RED	THYMUS - HEMORRHAGE

Animal ID: 353
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
OVARY - LEFT, ENLARGED, 5X5X4 MM	OVARY - NORMAL CORPORA LUTEA
OVARY - RIGHT, ENLARGED, 5X4X4 MM	OVARY - NORMAL CORPORA LUTEA
SKIN,APPLICATION SITE - CRUST, 1X1 MM, SINGLE/BLACK	SKIN,APPLICATION SITE - EXUDATIVE SCAB CONTAINS BLOOD

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3
STUDY NUMBER: 1052SN3
SEX: FEMALE
GROUP: LOW: (0.25 w/w%)

Animal ID: 368
Animal Fate: Terminal sacrifice
Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
THYMUS - PIGMENTATION, RED	THYMUS - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - CRUST	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 369
Animal Fate: Terminal sacrifice
Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 2X2 MM, MULTIPLE	SKIN,APPLICATION SITE - EXUDATIVE SCAB

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: FEMALE — GROUP: MID-LOW: (0.55 w/w%)

Animal ID: 386
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
UTERUS - BILATERAL, DILATATION	UTERUS - NOT REQUIRED BY PROTOCOL

Animal ID: 388
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
LIVER - CAUDATE LOBE, MASS, 18X12X4 MM, MOTTLED	LIVER - NOT REQUIRED BY PROTOCOL

Animal ID: 390
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 1X1 MM, RED	SKIN,APPLICATION SITE - NO CORRESPONDING LESION

Animal ID: 392
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 1X2 MM, MULTIPLE, (M9)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 395
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
OVARY - LEFT, CYST, 2X2 MM, CLEAR	OVARY - NOT REQUIRED BY PROTOCOL

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: FEMALE — GROUP: MID: (1 w/w%)

Animal ID: 406
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:
SKIN,APPLICATION SITE - CRUST, 15X10 MM, MULTIPLE, (M8)

Related Histopathology:
SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 407
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:
SKIN,APPLICATION SITE - CRUST, 1X1 MM, MULTIPLE, (M9)

Related Histopathology:
SKIN,APPLICATION SITE - NO CORRESPONDING LESION

Animal ID: 408
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:
SKIN,APPLICATION SITE - CRUST, 1X1 MM, (M8)

Related Histopathology:
SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 410
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:
SKIN,APPLICATION SITE - CRUST, 8X3 MM, MULTIPLE, (M8)

Related Histopathology:
SKIN,APPLICATION SITE - EXUDATIVE SCAB

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: FEMALE — GROUP: MID: (1 w/wt)

Animal ID: 411
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 1X2 MM, MULTIPLE	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 412
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 1X1 MM, (M9)	SKIN,APPLICATION SITE - NO CORRESPONDING LESION

Animal ID: 414
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 1X1 MM, MULTIPLE, RED	SKIN,APPLICATION SITE - EXUDATIVE SCAB; HEMORRHAGE

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: FEMALE — GROUP: MID-HIGH: (3 w/w%)

Animal ID: 426
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 12X5 MM, MULTIPLE, (M9)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 427
Animal Fate: Natural death — Days on Test: 7

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - EXUDATIVE SCAB
SKIN,APPLICATION SITE - LESION, (MULTIPLE SCABS)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 428
Animal Fate: Natural death — Days on Test: 14

Reference to Necropsy Record:	Related Histopathology:
LUNG - PARENCHYMA, PIGMENTATION, RED	LUNG - CONGESTION
SKIN,APPLICATION SITE - LESION, (SCALY)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 429
Animal Fate: Natural death — Days on Test: 7

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - LESION, (MULTIPLE SCABS)	SKIN,APPLICATION SITE - EXUDATIVE SCAB

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TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: FEMALE — GROUP: MID-HIGH: (3 w/w%)

Animal ID: 430
Animal Fate: Natural death — Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - LESION, (SCALY)	SKIN,APPLICATION SITE - EXUDATIVE SCAB
OVARY - BILATERAL, PIGMENTATION, RED	OVARY - CONGESTION

Animal ID: 431
Animal Fate: Natural death — Days on Test: 15

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, BROWN	SKIN,APPLICATION SITE - EXUDATIVE SCAB; NECROSIS

Animal ID: 432
Animal Fate: Terminal sacrifice — Days on Test: 30

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - CRUST, 7X8 MM, MULTIPLE	SKIN,APPLICATION SITE - EXUDATIVE SCAB

Animal ID: 433
Animal Fate: Natural death — Days on Test: 4

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - THICK	SKIN,APPLICATION SITE - NECROSIS
SKIN,APPLICATION SITE - PIGMENTATION, RED	SKIN,APPLICATION SITE - CONGESTION

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

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CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3 — STUDY NUMBER: 1052SN3
SEX: FEMALE — GROUP: MID-HIGH: (3 w/w%)

Animal ID: 434
Animal Fate: Natural death — Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NO CORRESPONDING LESION

Animal ID: 435
Animal Fate: Natural death — Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NO CORRESPONDING LESION

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3
SEX: FEMALE
STUDY NUMBER: 1052SN3
GROUP: HIGH: (5 w/w%)

Animal ID: 446
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
OVARY - BILATERAL, PIGMENTATION, RED	OVARY - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 447
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

Animal ID: 448
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
OVARY - BILATERAL, PIGMENTATION, RED	OVARY - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, RED	LUNG - NOT REQUIRED BY PROTOCOL
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

Animal ID: 449
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - NOT REQUIRED BY PROTOCOL

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FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3
STUDY NUMBER: 1052SN3
SEX: FEMALE
GROUP: HIGH: (5 w/wt)

Animal ID: 450
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
OVARY - BILATERAL, PIGMENTATION, RED	OVARY - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 451
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
OVARY - BILATERAL, PIGMENTATION, RED	OVARY - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 452
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:	Related Histopathology:
SKIN,APPLICATION SITE - PIGMENTATION, DARK	SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL
OVARY - BILATERAL, PIGMENTATION, RED	OVARY - NOT REQUIRED BY PROTOCOL
LUNG - PARENCHYMA, PIGMENTATION, DARK RED	LUNG - NOT REQUIRED BY PROTOCOL

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PATHOLOGY ASSOCIATES INTERNATIONAL
FOUR-WEEK DERMAL TOXICITY STUDY OF
TETRAMETHYLAMMONIUM HYDROXIDE (TMAH) IN RATS

IIT RESEARCH INSTITUTE PROJECT NUMBER 1052 STUDY NUMBER 3

CORRELATION OF GROSS & MICRO

STUDY ID: 1052 SN3
SEX: FEMALE
STUDY NUMBER: 1052SN3
GROUP: HIGH: (5 w/wt)

Animal ID: 453
Animal Fate: Natural death
Days on Test: 9

Reference to Necropsy Record:
SKIN,APPLICATION SITE - LESION, (SCALY)

Related Histopathology:
SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

Animal ID: 454
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:
SKIN,APPLICATION SITE - PIGMENTATION, DARK

LUNG - PARENCHYMA, PIGMENTATION, DARK

Related Histopathology:
SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

LUNG - NOT REQUIRED BY PROTOCOL

Animal ID: 455
Animal Fate: Natural death
Days on Test: 2

Reference to Necropsy Record:
SKIN,APPLICATION SITE - PIGMENTATION, DARK

LUNG - PARENCHYMA, PIGMENTATION, DARK, RED

Related Histopathology:
SKIN,APPLICATION SITE - NOT REQUIRED BY PROTOCOL

LUNG - NOT REQUIRED BY PROTOCOL

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SECTION VI

QUALITY ASSURANCE STATEMENT

Appendix R

QUALITY ASSURANCE STATEMENT

This histopathology project was inspected and audited by the PAI Quality Assurance Unit (QAU) as required by the Good Laboratory Practice (GLP) standards promulgated by the Environmental Protection Agency. The pathology narrative report is an accurate reflection of the recorded data. 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
07/01/99	Staining and Coverslipping	07/01/99
09/01/99	Individual Animal Data	09/01/99
09/01/99	Draft Pathology Report	09/01/99
09/13/99	Revised Draft Pathology Report	09/13/99
05/04/00	Final Pathology Report	05/04/00

Marie T. Dalcamo
Quality Assurance Unit
PAI Illinois Division

05/04/00
Date