



8EHQ-0309-17457A
DCN: 88090000181



RECEIVED
03-19-2009

March 19, 2009

09 MAR 27 AM 10:38

Certified Mail, 7008 1830 0002 0726 5791
Return Receipt Requested

Document Processing Center (7407M)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001



RE: Tetramethylammonium chloride, Dermal Toxicity
CAS Registry Number: 75-57-0

Dear Sir/Madam:

Sachem is submitting the attached toxicological testing under Section 8(e) of TSCA in an abundance of caution. Our investigation indicates that this toxicological information regarding the risks associated with dermal exposure of rabbits to TMAC may be new to EPA, and, although there is little risk of dermal exposure to humans, the results indicate a moderate level of risk.

To determine the potential for dermal toxicity of tetramethylammonium chloride a study complying with the standards set forth in OECD Guidelines for Testing Chemicals, Number 402 was conducted.

Initially, five healthy male and five healthy female New Zealand White rabbits were dosed dermally with Tetramethylammonium chloride, 98% at 500 mg/kg of body weight. Four of the ten rabbits survived the 500 mg/kg dose. Predeath physical signs included lethargy and wetness of the nose and mouth area. Necropsy results revealed abnormalities of the treated skin area, lungs, intestines, spleen, thymus and pancreas. Subsequently, an additional five males and five females were dosed at 200 mg/kg of body weight. All the rabbits survived the 200 mg/kg dose.

It was concluded the dermal LD₅₀ of Tetramethylammonium chloride, 98% is greater than 200 mg/kg but less than 500 mg/kg of body weight.

Questions may be directed to the undersigned at (512) 912-4412.

Sincerely,

Bryan M. Hale
ChemStewards Coordinator



Enclosure

Contains No CBI

CONTAINS NO CBI

318177

MB Research Laboratories

RECEIVED
JUL 1 2007

08 MAR 27 AM 10:38

1765 Wentz Road
P.O. Box 178
Spinnerstown, PA 18968
phone (215) 536-4110
fax (215) 536-1816

VOLUME II

Study Title : Acute Dermal Toxicity/LD 50 in Rabbits

Test Article : Tetramethylammonium Chloride, 98% (DEZ5-42),
Lot/batch #DEZ5-42

Author : Albert C. Gilotti, Ph.D., Study Director

Study Completed On : August 14, 2007

Performing Laboratory : MB Research Laboratories
1765 Wentz Road
P.O. Box 178
Spinnerstown, PA 18968

MB Research Project # : MB 07-15724.02

MB Research Protocol # : 2100-01

Sponsor : Sachem
821 E. Woodward St.
Austin, TX 78704

Citation : Albert C. Gilotti, Ph.D. (2007)
Unpublished Report by MB Research
Laboratories

MB Research Laboratories

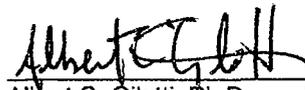
Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride, 98%
(DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

GOOD LABORATORY PRACTICES COMPLIANCE STATEMENT

This study was conducted in accordance with the Good Laboratory Practices of the EPA, 40 CFR 160 and 792, FDA 21 CFR 58 and as specified in Principles of Good Laboratory Practices, published by the Organization for Economic Cooperation & Development (OECD), 1997 with the following exception:

The test article characterization, supplied by the sponsor prior to study initiation, was not conducted under Good Laboratory Practices.

STUDY DIRECTOR :

 Aug 14 07
Albert C. Gilotti, Ph.D. Date
MB RESEARCH LABORATORIES

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride, 98%
(DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

GOOD LABORATORY PRACTICES COMPLIANCE STATEMENT

This study was conducted in accordance with the Good Laboratory Practices of the EPA, 40 CFR 160 and 792, FDA 21 CFR 58 and as specified in Principles of Good Laboratory Practices, published by the Organization for Economic Cooperation & Development (OECD), 1997 with the following exception:

The test article characterization, supplied by the sponsor prior to study initiation, was not conducted under Good Laboratory Practices.

STUDY DIRECTOR :

 Aug 14 '07
Albert C. Gilotti, Ph.D. Date
MB RESEARCH LABORATORIES

MB Research Laboratories

PROJECT NUMBER : MB 07-15724.02
TEST ARTICLE : Tetramethylammonium Chloride, 98% (DEZ5-42),
Lot/batch #DEZ5-42
SPONSOR : SACHEM
TITLE : Acute Dermal Toxicity/LD 50 in Rabbits
PROTOCOL # : 2100-01

A B S T R A C T

Objective: To determine the potential for toxicity of the test article when applied dermally. This study was designed to comply with the standards set forth in OECD Guidelines for Testing Chemicals, Number 402, adopted February 24, 1987.

Method Synopsis: Initially, five healthy male and five healthy female New Zealand White rabbits were dosed dermally with Tetramethylammonium Chloride, 98% (DEZ5-42), Lot/batch #DEZ5-42 at 500 mg/kg of body weight. Since compound related mortality occurred at this level, an additional five males and five females were dosed at 200 mg/kg of body weight. The test article was kept in contact with the skin for 24 hours. Dermal responses were recorded at 24 hours postdose and on days 7 and 14. Animals were observed for toxicity and pharmacological effects at 1, 2 and 4 hours postdose and once daily for 14 days. All animals were observed twice a day for mortality. Body weights were recorded pretest, weekly and at death or termination in the survivors. All animals were examined for gross pathology. Abnormal tissues were preserved in 10% neutral buffered formalin for possible future histological examination.

Summary:

500 mg/kg: Four of ten animals survived the 500 mg/kg dermal dose. Deaths occurred within 22 hours post dose. Predeath physical signs included lethargy and wetness of the nose/mouth area. Necropsy results revealed wetness of the nose/mouth area and abnormalities of the treated skin area, lungs, intestines, spleen, thymus and pancreas.

Instances of wetness of the nose/mouth area, lethargy, few feces and diarrhea were noted in the survivors. Dermal effects were absent throughout the study. Necropsy results revealed abnormalities of the thymus and kidneys among three of the survivors; one survivor appeared normal at necropsy.

200 mg/kg: All animals survived the 200 mg/kg dermal dose. Instances of diarrhea, few feces and soiling of the anogenital area were noted during the study. Dermal effects ranged from absent to very slight on Day 1 and were absent on Days 7 and 14. Body weight changes were normal. Necropsy results revealed abnormalities of the kidneys in one animal. Necropsy results were normal in all other animals.

Conclusion: The dermal LD₅₀ of Tetramethylammonium Chloride, 98% (DEZ5-42), Lot/batch #DEZ5-42 is greater than 200 mg/kg, but less than 500 mg/kg of body weight.

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride,
98% (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

OBJECTIVE

To determine the potential for toxicity of the test article when applied dermally. This study was designed to comply with the standards set forth in OECD Guidelines for Testing Chemicals, Number 402, adopted February 24, 1987.

TEST ARTICLE

Identity : Tetramethylammonium Chloride, 98% (DEZ5-42), Lot/batch #DEZ5-42
Test Article
Characterization : See Appendix A for Test Article Characterization and Final Lot Analysis.
Stability : The test article is stable according to the Test Article Characterization.
Supplied By : Sachem
Date Received : 05/08/07
Storage : Room temperature and humidity
Description : White crystals
Specific Gravity : Not applicable
Sample Preparation : The test article was individually weighed and moistened with a 0.4 to 1.4 ml of distilled water to form a paste.

TEST DATES

Study Initiation (date protocol signed) : 05/30/07
Experimental Start Date (1st exposure to test substance) : 05/31/07
Experimental Term Date (last date data collected) : 07/04/07
Draft Report Signed (if applicable) : 07/27/07
Final Report Signed (study completion) : 08/14/07

EXPERIMENTAL DESIGN

Test Animals

Animals were received from Millbrook Breeding Labs, Amherst, MA on 05/23/07 & 06/06/07. Following an equilibration period of at least one week, ten healthy male and ten non-pregnant and nulliparous female New Zealand White rabbits were randomly assigned to the treatment group using standard methods of randomization.

The animals were born weeks of 03/04/07 & 03/18/07. The pretest body weight range was 2.5 - 2.8 kg for males and 2.4 - 2.8 kg for females. The weight variation of the animals used did not exceed $\pm 20\%$ of the mean weight.

The animals were identified by cage notation and a uniquely numbered metal eartag and housed 1/cage in suspended wire cages. Bedding was placed beneath the cages and changed at least three times/week. Fresh PMI Rabbit Chow (Diet #5321) was provided daily. Water was freely available at all times. The animal room, reserved exclusively for rabbits on acute tests, was temperature controlled, had a 12 hour light/dark cycle, and was kept clean and vermin free.

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride,
98% (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

EXPERIMENTAL DESIGN (continued)

Site Preparation

The day prior to application of the test article, the dorsal area of the trunk of each animal was clipped free of hair. The prepared site was approximately 10% of the body surface and remained intact.

Dosing

The test article was moistened with 0.4 to 1.4 ml of distilled water to form a paste and applied to the prepared site under a four layered surgical gauze patch at a dose level of 200 and 500 mg/kg. The doses were based on the dry weight of the test article. Gentle pressure was applied to the gauze to aid in the distribution of the test substance over the prepared site. The torso was wrapped with plastic in a semi-occlusive manner and was secured with non-irritating tape. The test article remained in contact with the skin for 24 hours at which time the wrappings were removed. Residual test article was removed by gently washing with tap water/distilled water.

Type and Frequency of Observations

In vivo - The test sites were scored for dermal irritation at 24 hours postdose and on days 7 and 14 using the numerical Draize scoring code below. The skin was also evaluated for ulceration and necrosis or any evidence of tissue destruction.

Erythema & Eschar	
No erythema	0
Very slight erythema (barely perceptible)	1
Well defined erythema	2
Moderate to severe erythema	3
Severe erythema (beet redness) to slight eschar formation (injuries in depth)	4
Edema	
No edema	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising)	2
Moderate edema (raised approximately 1.0 mm)	3
Severe edema (raised more than 1.0 mm, extending beyond the area of exposure)	4

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride,
98% (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

RESULTS & DISCUSSION

1. Mortality, Body Weights, Systemic Observations & Necropsy Findings (Tables 1 - 3)

500 mg/kg: Four of ten animals survived the 500 mg/kg dermal dose. Deaths occurred within 22 hours post dose. Predeath physical signs included lethargy and wetness of the nose/mouth area. Necropsy results revealed wetness of the nose/mouth area and abnormalities of the treated skin area, lungs, intestines, spleen, thymus and pancreas.

Instances of wetness of the nose/mouth area, lethargy, few feces and diarrhea were noted in the survivors. Dermal effects were absent throughout the study. Necropsy results revealed abnormalities of the thymus and kidneys among three of the survivors; one survivor appeared normal at necropsy.

200 mg/kg: All animals survived the 200 mg/kg dermal dose. Instances of diarrhea, few feces and soiling of the anogenital area were noted during the study. Dermal effects ranged from absent to very slight on Day 1 and were absent on Days 7 and 14. Body weight changes were normal. Necropsy results revealed abnormalities of the kidneys in one animal. Necropsy results were normal in all other animals.

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride,
98% (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

CONCLUSION

The dermal LD₅₀ of Tetramethylammonium Chloride, 98% (DEZ5-42), Lot/batch #DEZ5-42 is greater than 200 mg/kg but less than 500 mg/kg of body weight.

FINAL REPORT

Approved by:


Albert C. Gilotti, Ph.D.
Study Director

 Aug 14 '07
Date

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride, 98%
 (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

Table 1: Body Weights, Dose Weight and Dermal Observations

Dose Level: 500 mg/kg

An. #	Sex	Dose Weight in g	Body Weight in kg			24 Hours		Day 7		Day 14		% Remaining at 24 hours
			Day 0	Day 7	Day 14	Erythema	Edema	Erythema	Edema	Erythema	Edema	
G9762	M	1.25	2.5									
G9764	M	1.35	2.7									
G9766	M	1.25	2.5									
G9768	M	1.40	2.8	2.9	3.2	0	0	0*	0	0*	0	10%
G9769	M	1.25	2.5									
	MEAN		2.6									
	S.D.		0.1									
	#		5									
G9794	F	1.30	2.6	2.7	3.0	0	0	0*	0	0*	0	10%
G9796	F	1.40	2.8									
G9797	F	1.30	2.6									
G9798	F	1.20	2.4	2.6	2.9	0	0	0	0	0*	0	10%
G9800	F	1.20	2.4	2.5	2.8	0	0	0*	0	0*	0	10%
	MEAN		2.6	2.6	2.9							
	S.D.		0.2	0.1	0.1							
	#		0	5	3							

% Remaining = a visual estimate of the amount of material remaining on the skin, gauze and binding at 24 hours, after the binding was removed.

* = reclipped

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride, 98%
 (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

Table 1: Body Weights, Dose Weight and Dermal Observations (cont'd)

Dose Level: 200 mg/kg

An. #	Sex	Dose Weight in g	Body Weight in kg			24 Hours		Day 7		Day 14		% Remaining at 24 hours
			Day 0	Day 7	Day 14	Erythema	Edema	Erythema	Edema	Erythema	Edema	
G9975	M	0.52	2.6	2.7	2.9	0	0	0*	0	0	0	5%
G9976	M	0.56	2.8	3.0	3.2	1	0	0*	0	0	0	5%
G9977	M	0.50	2.5	2.7	2.8	1	0	0*	0	0*	0	5%
G9978	M	0.52	2.6	2.9	3.1	0	0	0	0	0*	0	5%
G9983	M	0.52	2.6	2.9	3.1	0	0	0	0	0*	0	5%
	MEAN		2.6	2.8	3.0							
	S.D.		0.1	0.1	0.2							
	#		5	5	5							
H4	F	0.48	2.4	2.7	2.8	0	0	0*	0	0	0	5%
H11	F	0.52	2.6	2.8	2.9	0	0	0*	0	0*	0	5%
H12	F	0.50	2.5	2.7	2.9	0	0	0*	0	0	0	5%
H13	F	0.50	2.5	2.6	3.0	0	0	0*	0	0*	0	5%
H14	F	0.52	2.6	2.8	2.9	0	0	0*	0	0*	0	5%
	MEAN		2.5	2.7	2.9							
	S.D.		0.1	0.1	0.1							
	#		5	5	5							

% Remaining = a visual estimate of the amount of material remaining on the skin, gauze and binding at 24 hours, after the binding was removed.

* = reclipped

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride, 98%
 (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

Table 2: Systemic Observations

Dose Level: 500 mg/kg

TIME PERIODS	ANIMAL # & SEX									
	G9762 M	G9764 M	G9766 M	G9768 M	G9769 M	G9794 F	G9796 F	G9797 F	G9798 F	G9800 F
Hour 1			Z*	1	Z*			B,1		
Hour 2				B,1				Z		
Hour 4		Z**		1						
Day 1	Z (2.5 kg)						Z (2.8 kg)		D	
Day 2						X				
Day 3										
Day 4										
Day 5										
Day 6						X			X	X
Day 7										
Day 8										
Day 9										
Day 10										
Day 11										
Day 12										
Day 13										
Day 14										

No entry indicates animal appeared normal at that observation period. 1 = nose/mouth area wet B = lethargy D = diarrhea X = few feces Z = dead
 * = animals dead prior to one hour observation ** = animal found dead slightly after 4 hour observation

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
 Project # : MB 07-15724.02
 Test Article : Tetramethylammonium Chloride, 98%
 (DEZ5-42), Lot/batch #DEZ5-42
 Protocol : 2100-01

Table 2: Systemic Observations (continued)

Dose Level: 200 mg/kg

TIME PERIODS	ANIMAL # & SEX									
	G9975 M	G9976 M	G9977 M	G9978 M	G9983 M	H4 F	H11 F	H12 F	H13 F	H14 F
Hour 1										
Hour 2										
Hour 4										
Day 1				D		D			D	
Day 2										
Day 3										
Day 4				X						
Day 5										
Day 6										
Day 7										
Day 8										
Day 9										D
Day 10						X				
Day 11										X
Day 12						T				X
Day 13										T
Day 14										

No entry indicates animal appeared normal at that observation period. D = diarrhea X = few feces T = soiling of the anogenital area

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride, 98%
 (DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

Table 3: Necropsy Observations

Dose Level: 500 mg/kg

Animal number	G9762	G9764	G9766	G9768	G9769	G9794	G9796	G9797	G9798	G9800
Sex	M	M	M	M	M	F	F	F	F	F
Death/Sacrifice	D	D	D	S	D	S	D	D	S	S
Normal						X				
Treated skin abnormalities			1							
Lungs: red areas	2						3			
Intestines: red areas							2			
Intestines: distended with fluid							3			
Intestines: distended with gas		1						1		
Intestines: pale		1								
Nose/mouth area: wet	1		1		1		1	2		
Spleen: pale	2	1					1			
Thymus: dark areas	2			2			3		1	
Pancreas: red spot	1									
Kidneys: dark areas				1					1	2
Kidneys: pale areas				1						2

CODES: D = death 1= slight or scattered
 S = sacrifice 2= moderate or few
 X = observed 3= pronounced or many

MB Research Laboratories

Study Title : Dermal Toxicity in Rabbits
Project # : MB 07-15724.02
Test Article : Tetramethylammonium Chloride, 98%
(DEZ5-42), Lot/batch #DEZ5-42
Protocol : 2100-01

QUALITY ASSURANCE EVALUATION

The Quality Assurance Unit has inspected a critical phase of this study, audited the raw data and the report and determined that the methods and results contained herein accurately reflect the raw data. No deviations from the approved protocol or Standard Operating Procedures were made without proper authorization and documentation. A summary of the compliance inspections is presented below.

Date of Inspection	Phase	Performed By	Date Findings Reported to	
			Mgmt.	Sty. Dir.
05/31/07	Dosing administration	Erin Range	08/13/07	08/14/07
07/18/07	Raw data audit	William J. Kintigh	08/13/07	08/14/07
07/26/07	Draft report audit	William J. Kintigh	08/13/07	08/14/07
08/13/07	Final report audit	Erin Range	08/13/07	08/14/07


Erin Range, B.S., LATG Date
Quality Assurance Unit

MB Research Laboratories

1765 Wentz Road
P.O. Box 178
Spinnerstown, PA 18968
phone (215) 536-4110
fax (215) 536-1816

TEST ARTICLE CHARACTERIZATION INFORMATION

In compliance with Good Laboratory Practice (GLP) regulations, a characterization of the test article is required and should include identity, strength, purity, composition, stability and uniformity. This data must be reviewed by the Study Director prior to study initiation and will be included in the final report. (EPA 40 CFR 160.105 and 792.105; FDA 21 CFR 58.105, OECD 6.2).

In addition, the test article characterization should be performed in compliance with the Good Laboratory Practices.

Any exceptions to the GLP requirements will be indicated in the Compliance Statement of the final report.

Accordingly, please supply the following information for each test article submitted:

Test Article Identity : (DEZ 5-42) tetramethylammonium chloride (TMAC)
Strength : 100.42 wt%
Purity : _____
Composition : _____
Stability : stable ; decomposition @ 275°C
Uniformity : homogeneous, white, crystals

This characterization **was** conducted under GLPs (or)

This characterization **was not** conducted under GLPs

BY: Dora E Zapata
(signature)

FOR: Sachem, Inc.
(company)

4/23/07
(date)



SACHEM

Final Lot Analysis

316 - Tetramethylammonium Chloride, 98% Crystals

In Inventory? Yes

Entered Date: 02/12/2007

Analysis Date: 02/11/2007

Customer:

Lot Number: C70687X39707

Lab: C70987

Retained Sample: Yes

Sample ID: 02/09/2007

Is there an "X" in the Final Lot Analysis number? Yes No

Please list the reason for "X":

preissued lot#

Test	Test Details	Measure	Analysis Result	Detection Limit
Date of Manufacture			02/09/2007	
Assay		wt%	100.42	
Last drum assay		wt%	100.39	
Me3N	(Trimethylamine)	wt%	0.05	0.04
Me3N.HCl	(Trimethylamine Hydrochloride)	wt%	0.05	0.04
Fe	(Iron)	ppm	0.15	0.4
K	(Potassium)	ppm	0.15	
K + Na	(Potassium + Sodium)	ppm	0.454	0.4
Na	(Sodium)	ppm	0.304	0.4
Appearance			pass	
H2O	Karl Fischer Identification (Water)	wt%	0.12	0.01