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Chemical Category ETHYLAMINE, TRIETHYLAMINE AND DIETHYLAMINE			

8(e)

5947

CAP

(COMPLIANCE AUDIT PROGRAM)

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88920004593

Attn: Section 8(e) Coordinator (CAP Agreement)

Re: CAP Agreement Identification No. 8ECAP-0110

Dear Sir or Madam:

Union Carbide Corporation ("Union Carbide") herewith submits the following report pursuant to the terms of the TSCA §8(e) Compliance Audit Program and Union Carbide's CAP Agreement dated August 14, 1991 (8FCAP-0110). This report describes acute dermal toxicity studies with ethylamine (CASRN 75-04-7), triethylamine (CASRN 121-44-8); and diethylamine (CASRN 109-89-7).

"Primary Dermal Irritation Study In Albino Rabbits Administered Test Articles Ethylamine, Triethylamine and Diethylamine"; Bio Research Laboratories Ltd., Project No. 51305, January 13, 1986.

A complete summary of this report is attached.

Previous TSCA Section 8(e) or "FYI" Submission(s) related to this substance are:

(None)

Previous PMN submissions related to this substance are: (None)

This information is submitted in light of EPA's current guidance. Union Carbide does not necessarily agree that this information reasonably supports the conclusion that the subject chemical presents a substantial risk of injury to health or the environment.

In the attached report the term "CONFIDENTIAL" may appear. This precautionary statement was for internal use at the time of issuance of the report. Confidentiality is hereby waived for purposes of the needs of the Agency in assessing health and safety information. The Agency is advised, however, that the publication rights to the contained information are the property of Union Carbide.

Yours truly,



William C. Kuryla, Ph.D.
Associate Director
Product Safety
(203/794-5230)

WCK/cr

Attachment (3 copies of cover letter, summary, and report)

SUMMARY



BIO-RESEARCH LABORATORIES LTD.

PROJECT NO. 51305

PRIMARY DERMAL IRRITATION STUDY IN ALBINO RABBITS ADMINISTERED
TEST ARTICLES ETHYLAMINE, TRIETHYLAMINE
AND DIETHYLAMINE

SUMMARY

PROJECT NO. 51305

SUMMARY

Under contract to Union Carbide Canada Limited, Bio-Research Laboratories Ltd., Senneville, Quebec, Canada, has conducted a primary dermal irritation study in 3 albino rabbits each administered one of the following test articles: ethylamine, triethylamine and diethylamine (Bio-Project No. 51305).

This study was conducted in accordance with the requirements of Transport Canada and the study conduct complied with the EPA (TSCA) "Good Laboratory Practice" regulations (40 CFR Part 792).

Three test articles (ethylamine, triethylamine and diethylamine) were administered once under gauze pads to 3 intact skin sites on the dorsum of 3 anesthetized albino rabbits (one test article/animal). Three minutes post-application, one gauze pad was removed, the residual test article was wiped off and an evaluation of the dermal irritation and of corrosivity was performed. Similar readings were performed 60 minutes post-treatment using the second test site. Evaluation of the dermal irritation and of corrosiveness was performed on one rabbit (ethylamine) at approximately 30 minutes post-treatment using the second test site. On each occasion, the scoring of irritation was performed according to the methods of Draize et al., and each test article was classified according to the Transport of Dangerous Goods Code No. 3.25- 3.26.

Three minutes post-application, two animals (administered diethylamine and triethylamine, respectively) were killed because of corrosivity and were discarded without necropsy. One rabbit (ethylamine) died approximately 30 minutes post-application due to the anesthetic. Evidence of corrosivity was observed at this time.

CONCLUSION

Following topical administration to intact rabbit skin, triethylamine and diethylamine were found to be "Packing Group I" compounds according to the Canadian Transport of Dangerous Goods Code (Appendix 2), since they produced necrosis (sloughing of skin) 3 minutes post-application. Ethylamine was found to be a "Packing Group II" compound according to the Canadian Transport of Dangerous Goods Code since it produced necrosis (sloughing of skin) at approximately 30 minutes post-application.



BIO-RESEARCH LABORATORIES LTD.

CONFIDENTIAL RESEARCH REPORT

PRIMARY DERMAL IRRITATION STUDY IN
ALBINO RABBITS ADMINISTERED
TEST ARTICLES ETHYLAMINE,
TRIETHYLAMINE AND
DIETHYLAMINE

by

Colin B. Bier, Ph.D.

For: Union Carbide Canada Limited
10555 Metropolitan Blvd.
Montreal East, Quebec

Project No.: 51305

Date: January 13, 1986

MONTREAL

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BIO-RESEARCH LABORATORIES LTD.

PROJECT NO. 51305

PRIMARY DERMAL IRRITATION STUDY IN ALBINO RABBITS ADMINISTERED
TEST ARTICLES ETHYLAMINE, TRIETHYLAMINE
AND DIETHYLAMINE

This research was conducted at Bio-Research Laboratories on November 27, 1985
under the direction of:

C. B. Bier

C. B. Bier, Ph.D.
Director, Division of Experimental Toxicology
and Clinical Pathology
Study Director

14 January 1986

Date

With the participation of the following:

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SUMMARY

Under contract to Union Carbide Canada Limited, Bio-Research Laboratories Ltd., Senneville, Quebec, Canada, has conducted a primary dermal irritation study in 3 albino rabbits each administered one of the following test articles: ethylamine, triethylamine and diethylamine (Bio-Project No. 51305).

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Three minutes post-application, two animals (administered diethylamine and triethylamine, respectively) were killed because of corrosivity and were discarded without necropsy. One rabbit (ethylamine) died approximately 30 minutes post-application due to the anesthetic. Evidence of corrosivity was observed at this time.

CONCLUSION

Following topical administration to intact rabbit skin, triethylamine and diethylamine were found to be "Packing Group I" compounds according to the Canadian Transport of Dangerous Goods Code (Appendix 2), since they produced necrosis (sloughing of skin) 3 minutes post-application. Ethylamine was found to be a "Packing Group II" compound according to the Canadian Transport of Dangerous Goods Code since it produced necrosis (sloughing of skin) at approximately 30 minutes post-application.

INTRODUCTION

This study was undertaken to determine the relative dermal irritancy and corrosivity of test articles ethylamine, triethylamine and diethylamine when administered topically to the intact skin of albino rabbits.

Description of Test Article

Test article ethylamine was supplied by Union Carbide Ltd.

Identity/Code	: Ethylamine, 70%
Batch Number	: TF-4-010688 5031 RN
Consistency	: Liquid
Color	: Clear
Purity	: 70-72%
Strength	: Not supplied by Sponsor
Stability	: Expiry date not supplied by Sponsor
Storage	: Room temperature, dark
Handling Precautions	: Routine laboratory precautions plus respirator and safety glasses
pH	: 14

Test article triethylamine was supplied by Union Carbide Ltd.

Identity/Code	: Triethylamine
Batch Number	: TF-4-012273 5190 HT
Consistency	: Liquid
Color	: Clear
Purity	: 99.5% by weight minimum
Strength	: Not supplied by Sponsor
Stability	: Expiry date not supplied by Sponsor
Storage	: Room temperature, dark
Handling Precautions	: Routine laboratory precautions plus respirator and safety glasses
pH	: 14

Test article diethylamine was supplied by Union Carbide Ltd.

Identity/Code	:	Diethylamine
Batch Number	:	TF-4-012482 5210 RN
Consistency	:	Liquid
Color	:	Clear
Purity	:	100%
Strength	:	Not supplied by Sponsor
Stability	:	Expiry date not supplied by Sponsor
Storage	:	Room temperature, dark
Handling Precautions	:	Routine laboratory precautions plus respirator and safety glasses
pH	:	10.8

Methods and Experimental Design

1. Test System

a) Specifications

Species	:	<u>Oryctolagus cuniculus</u>
Strain	:	New Zealand White
Body Weight	:	2.2 to 2.6 kg at dosing
Age	:	10 to 11 weeks on arrival.
No. of Animals*	:	3 males (plus one replacement)

*4 males were received, and utilized in this study.

b) Source of Supply of Test System

Maple Lane Rabbits
Box 377
Clifford, Ontario
NOG 1M0

c) Test System/Reason for Selection

1. This species is readily available from a reliable and trusted source.
2. This species is hardy and does not require complicated housing.
3. A large data base is available for this species.

4. The rabbit is the most widely recognized species used to predict skin irritation and/or corrosive properties of a test substance.
5. This species was requested by the Sponsor since this is a species of choice for conducting the test.

d) Housing and Maintenance

All rabbits were individually housed in stainless steel cages equipped with water bottles. Environmental conditions during the study were controlled and both temperature ($18.7 \pm 0.92^{\circ}\text{C}$) and relative humidity ($43.0 \pm 5.66\%$) were recorded twice daily throughout the study. A photoperiod of 12 hours light/12 hours dark was maintained throughout the study. Each rabbit was identified by a permanent individual number on the ventral surface of the pinnae. The study, animal and group numbers, dose, sex and study interval appeared on the outside of each cage to preclude animal mix-up subsequent to test system removal for test article administration, sanitation procedures, physical examination and other study-related reasons. Upon arrival at Bio-Research Laboratories Ltd., a staff veterinarian or his aide conducted a general physical examination of each rabbit.

All animals were acclimated for 7 days to allow them to become accustomed to the laboratory setting. During the acclimation and treatment periods, the animals were fed a standard commercial pelleted diet (Purina Certified Rabbit Chow 5322) and were supplied water ad libitum. The drinking water is periodically analyzed and found to be fit for human and animal intake.

Based upon current information about the test articles, there are no known contaminants in the food or water that can reasonably be expected to have interfered with the purpose or conduct of the study.

During the acclimation period and the study conduct, only professional and technical staff assigned to this study were permitted access to the animal room utilized in the housing of this study.

e) Method of Randomization

Animals were not randomized since only 3 males (plus one replacement) were used in the study.

f) Preparation

Animals were shaved at least 24 hours prior to test article application. Hair was removed from an area of the dorsum exposing approximately 10% of the body surface. Animals were anesthetized prior to test article application using a pre-anesthetic (mix of Atravet, Ketaset and atropine sulfate in solution) followed by an anesthetic (Somnotol).

2. Test Article Administrationa) Test Group

No. of Test Groups : 3
No. of Animals/Test Group: 1 male
Total No. of Animals : 3 males (plus one replacement)
Animal Nos. : 1012, 2012, 3012*, 3112
Control : Each animal served as its own control.

*Animal 3012 died prior to dosing due to anesthetic and was replaced by animal 3112.

b) Dose Frequency

Ethylamine, diethylamine and triethylamine were administered once, undiluted, to males 1012, 2012 and 3112, respectively.

c) Dosing

For each test article, a dose of 0.5 mL was applied under a gauze pad (approximately 2 x 2 cm) placed on each of 3 intact skin sites on the dorsum of one animal. Three minutes post-treatment, one gauze pad was removed, the residual test article was wiped off with a dry gauze pad and a reading was taken. No evidence of corrosivity was present in one animal (ethylamine) and this animal was maintained and a similar reading was performed at approximately 30 minutes using the second test site. Since there was evidence of corrosivity at three minutes post-treatment in the remaining two animals (diethylamine and triethylamine, respectively) these animals were then euthanized.

d) Route of Administration and Reason for Choice

The dermal route was selected to determine the potential dermal irritancy and corrosivity of test articles ethylamine, triethylamine and diethylamine in the New Zealand White rabbit. This route was utilized since this is a probable route of accidental exposure of man to the test articles.

3. Test System Observations Following Test Article Administration

Erythema and edema scores as well as evidence of corrosiveness were recorded at 3 minutes and approximately 30 minutes after dosing. Scorings of irritation and corrosiveness, respectively, were performed in accordance with the methods of Draize et al. (Assoc. of Food and Drug Officials of the U.S., Austin, Texas, 1959 - Appendix 1) and the Transport of Dangerous Goods (Canada Gazette, Part 2, Vol. 119, No. 3, Code No. 3.25 - 3.26, 1985 - Appendix 2).

4. Termination of Study

Subsequent to appraisal of dermal irritation on day 1, all surviving animals were killed by an overdose of T-61 (Hoechst), administered by intravenous injection, and were then discarded without necropsy.

5. Quality Assurance

The Quality Assurance Department of Bio-Research Laboratories Ltd. undertook and documented inspections and audits of the study during its conduct.

6. Archiving

All raw data, documentation, protocols and the final report are retained in the archives of Bio-Research Laboratories Ltd. in accordance with the Good Laboratory Practice regulations.

RESULTS AND DISCUSSION

Test articles ethylamine (pH = 14), triethylamine (pH = 14) and diethylamine (pH = 10.8) were each administered by topical patch application to 3 intact skin sites on 1 of 3 anesthetized albino rabbits at a dose of 0.5 mL per skin site.

The individual primary irritation scores (erythema/edema) of rabbits administered each test article are presented in Table No. 1.

When applied to intact skin, ethylamine produced well-defined erythema and very slight edema 3 minutes post-application. The skin became dark and necrotic with increased time (post 3 minutes). Triethylamine and diethylamine produced severe erythema (with sloughing of skin) 3 minutes post-application. Rabbit 1012 (ethylamine) died approximately 30 minutes post-application due to the anesthetic but was not replaced since evidence of corrosivity (sloughing of skin) was observed at this time. Both rabbit 2012 (diethylamine) and rabbit 3112 (triethylamine) were euthanized 3 minutes post-application because of corrosivity.

According to the Transport of Dangerous Goods Code of Canada, triethylamine and diethylamine are classified as "Packing Group I" compounds. Ethylamine is classified as a "Packing Group II" compound.

TABLE NO. 1

PRIMARY DERMAL IRRITATION
(ERYTHEMA/EDEMA)* SCORES IN NEW ZEALAND
WHITE RABBITS ADMINISTERED TEST ARTICLES
ETHYLAMINE, TRIETHYLAMINE
AND DIETHYLAMINE

PROJECT NO. 51305

ANIMAL NUMBER	TEST ARTICLE	TIME POSTAPPLICATION		
		3 MINUTES SITE A	60 MINUTES SITE B	4 HOURS SITE C
1012	Ethylamine	2/1++	4/1**	-
2012	Diethylamine	4/0+	-	-
3112	Triethylamine	4/0+	-	-

*Maximum erythema or edema score = 4.

**Animal died due to anesthetic approximately 30 minutes post-treatment.
Scoring performed prior to death.

+Sloughing of skin (corrosivity), animal euthanized post first scoring.

++Skin dark and necrotic with increased time (post 3 minutes).

EVALUATION OF SKIN REACTIONS
(According to Draize)

<u>Erythema</u>	<u>Score</u>
Very slight erythema, barely perceptible (edges of area not defined)	1
Well-defined erythema (pale red in color)	2
Moderate to severe erythema (definite red in color)	3
Severe erythema (beet or crimson red in color) and/or slight eschar formation (injuries in depth)	4
Total possible erythema score	4
<u>Edema</u>	
Barely perceptible, very slight edema (edges of area not defined)	1
Slight edema (edges of area not definable but definite raising)	2
Moderate edema (area well-defined and raised approximately 1 mm)	3
Severe edema (raised more than 1 mm and extending beyond area of exposure)	4
Total possible edema score	4
Maximum possible score	8

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APPENDIX NO. 2

CLASSIFICATION OF CORROSIVES
PACKING GROUPS

PROJECT NO. 51305

- Packing Group I - If visible necrosis of the skin tissue occurs after continuous contact for not more than 3 minutes.
- Packing Group II - If visible necrosis of the skin tissue occurs after continuous contact for more than 3 minutes but not more than 60 minutes.
- Packing Group III - If visible necrosis of the skin tissue occurs after continuous contact for more than 1 hour but not more than 4 hours.

Department of Transport, Canada

QUALITY ASSURANCE
STATEMENT

F815

In compliance with the Good Laboratory Practice Regulations, Study 51305 has been reviewed. The data presented in the final report accurately represent the data collected during the conduct of the study.

Dates of Inspection	Dates of Reports to Management and Study Director
November 27, 1985 January 10, 13, 1986	November 29, 1985 January 13, 1986

QUALITY ASSURANCE:

M. Alabekis
P. Sely

DATE: Jan 14/86

DATE: January 14, 1986

CERTIFICATE OF AUTHENTICITY

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