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UNION CARBIDE CORPORATION 39 OLD RIDGEBURY ROAD, DANBURY, CT 06817-0001

July 28, 1992

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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 (8ECAP-0110). This report describes a guinea pig sensitization study with aminoethylethanolamine (AEEA; CASRN 111-41-1).

"Guinea Pig Maximization Test: Test Material: Aminoethylethanolamine (AEEA)", Bio/dynamics, Project No. 5502-89, July 11, 1990.

A complete summary of this report is attached.

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

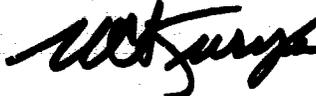
(None)

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/dynamics Inc.

Department of Toxicology

BIO/DYNAMICS PROJECT NO.: 5502-89

GUINEA PIG MAXIMIZATION TEST

TEST MATERIAL: Aminoethylethanolamine (AEEA)

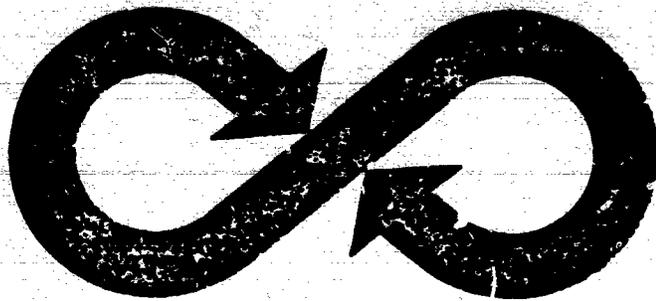
Submitted to: Union Carbide Corporation  
39 Old Ridgebury Road  
Danbury, Connecticut 06817-0001

Attn: Dr. Hon-Wing Leung

Date: July 11, 1990

**CONCLUSION**

Based on a 40% clear response, AEEA would be considered a moderate dermal sensitizer under conditions of this study. There was evidence of cross-sensitization to ethylenediamine, diethylenetriamine - high purity, and triethylenetetramine. Possible slight cross-sensitization to piperazine was also suggested.



**Bio/dynamics Inc.**

**Department of Toxicology**

**BIO/DYNAMICS PROJECT NO.: 5502-89**

**GUINEA PIG MAXIMIZATION TEST**

**TEST MATERIAL: Aminoethylethanolamine (AEEA)**

**Submitted to: Union Carbide Corporation  
39 Old Ridgebury Road  
Danbury, Connecticut 06817-0001**

**Attn: Dr. Hon-Wing Leung**

**Date: July 11, 1990**

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I. INTRODUCTION

This study was conducted for Union Carbide Corporation in order to evaluate the allergic contact sensitization potential of Aminoethylethanolamine (AEEA) in guinea pigs and to evaluate any potential for cross-sensitization to several structurally similar materials. This study was performed at Bio/dynamics, Inc., Mettlers Road, East Millstone, New Jersey 08875-2360, using procedures based on the method described by Bertil Magnusson, M.D., and Albert M. Kligman, M.D., Ph.D. in "The Identification of Contact Allergens by Animal Assay. The Guinea Pig Maximization Test," Journal of Investigative Dermatology, 57: 268-276 and in Allergic Contact Dermatitis in the Guinea Pig. Identification of Contact Allergens, Thomas, Springfield, IL, 1970.

This report has been reviewed by the Quality Assurance Unit of Bio/dynamics, Inc. to assure its conformance with the protocol and the raw data. All raw data and the original study protocol and final report will be retained on file in the Bio/dynamics, Inc. Archives.

II. EXPERIMENTAL DESIGN

Group	Test Material	Number of Animals	Concentration (%)					
			Induction			Topical	Challenge	Cross-Challenge
			Site 1	Site 2	Site 3			
IA	Aminoethylethanolamine (AEEA)	20 (10M, 10F)	a	5.0 <sup>b</sup>	5.0 <sup>c</sup>	50 <sup>b</sup>	25 <sup>b</sup>	25 <sup>b,f</sup>
IB	Aminoethylethanolamine (AEEA) (Irritation Control)	10 (5M, 5F) <sup>d</sup>	a	b	5.0 <sup>b,c</sup>	b	25 <sup>b</sup>	-
IC	Cross-Challenge Control	10 (5M, 5F) <sup>e</sup>	a	b	5.0 <sup>b,c</sup>	b	-	25 <sup>b,f</sup>

<sup>a</sup>Site 1 - animals received a 50% FCA/water emulsion.

<sup>b</sup>Vehicle=Distilled water.

<sup>c</sup>Site 3 - dose administered in a 50% FCA/water emulsion.

<sup>d</sup>Irritation control animals were also used for Bio/dynamics, Inc. Project Nos.: 5501-89 and 5614-89.

<sup>e</sup>Cross-Challenge animals were also used for Bio/dynamics, Inc. Project Nos.: 5496-89, 5497-89, 5498-89, 5501-89 and 5614-89.

Cross-challenged with:	Material	Concentration (in water)
	Ethylenediamine-UHP (EDA)	5%
	Diethylenetriamine-HP (DETA-HP)	25%
	Triethylenetetramine (TETA)	50%
	Aminoethylpiperazine (AEP)	25%
	Tetraethylenepentamine (TEPA)	50%
	Piperazine	25%

M=Male; F=Female.

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5502-89**III. DATES OF STUDY**

**Animal Receipt:** September 5, 1989

**Range-Finding:**  
**Intradermal:** September 21, 1989  
**Topical:** September 20, 1989

**Induction of Sensitization:**  
**Intradermal:** Day 0: September 26, 1989  
**Topical:** Day 7: October 3, 1989

**Challenge - Topical:** Day 21: October 17, 1989

**Evaluation of Response:** Days 23 and 24: October 19 & 20, 1989

**Cross-Challenge:** Day 28: October 24, 1989

**Evaluation of Response:** Days 30 and 31: October 26 & 27, 1989

**IV. STUDY PERSONNEL**

**Study Director:** Carol S. Auletta, B.A., D.A.B.T.

**Laboratory Supervisor:** Janet E. Trimmer, A.A.S., AALAS R.L.A.T.

**Technician-in-Charge:** Brian Luke, B.A., AALAS R.L.A.T.

**Study Monitor  
(Report Preparation):** Lynda C. Olsen, B.A., AALAS L.A.T.

**V. MATERIALS****A. Test and Control Materials:**

**1. Test Material:** Aminoethylethanoamine (AEEA)

**Description:** Clear liquid; slight yellow tint

**Date of Receipt:** September 19, 1989

**Received from:** Union Carbide Corporation

**Storage:** Room temperature

**Vehicle:** Distilled water

V. MATERIALS (cont.)A. Test and Control Materials (cont.):

2. **Adjuvant:** Freund's Complete Adjuvant (FCA)
- Description:** A mixture of paraffin oil and an emulsion with mycobacteria.
- Supplier:** Difco Laboratories  
Detroit, Michigan
- Storage:** Room temperature
3. **Positive Control:** Bio/dynamics has a historical base of data for animals tested with a known sensitizer (dinitrochlorobenzene) which demonstrates the susceptibility of this source of animals to dermal sensitization. Groups of animals are tested periodically. See Appendix C for historical positive control data.

4. **Cross-Challenge:**

<u>Material</u>	<u>Description</u>	<u>Receipt Date</u>
EDA	Clear liquid; very slight yellow tint	9/19/89
DETA-HP	Clear yellow liquid	9/19/89
TETA	Clear liquid	9/19/89
AEP	Clear liquid	9/19/89
TEPA	Yellowish liquid	9/25/89
Piperazine	White solid; clear liquid when melted	9/19/89

**Received from:** Union Carbide Corporation

**Storage:** Room temperature

**Vehicle:** Distilled water

B. Test Animals: Guinea Pigs

**Stock:** Hartley Albino

**Reason for Selection:** Standard laboratory animal for dermal sensitization studies. The Hartley Albino breed was used because of its availability and because of the existing historical data base for comparative evaluation.

**Supplier:** Hazleton Research Animals, Inc.  
Denver, Pennsylvania

V. MATERIALS (cont.)B. Test Animals (cont.)

- Number of Animals:**
1. Range-finding: 8 (4 males, 4 females)
  2. Sensitization Study:  
20 (10 males, 10 females)
  3. Irritation Controls:  
Challenge: 10 (5 males, 5 females)  
Cross-Challenge: 10 (5 males,  
5 females)
- Age:** 3-4 weeks at receipt  
5-6 weeks old at study initiation
- Pretest Weight Range  
(Sensitization Study  
Animals):** Males: 324 to 400 grams  
Females: 306 to 345 grams
- Equilibration Period  
(Sensitization Study  
Animals):** 21 days
- Observation:** All animals were checked for viability twice daily. Prior to assignment to study all animals received a physical examination to ascertain suitability for study.
- Husbandry:** Currently acceptable practices of animal husbandry were followed, e.g., Guide for the Care and Use of Laboratory Animals; NIH Publication No. 86-23 Revised 1985.
- Housing:** Individually in suspended stainless steel cages.
- Environmental  
Conditions:**
1. Temperature: monitored and recorded twice daily.
  2. Humidity: monitored and recorded daily.
  3. Light Cycle: 12 hours light, 12 hours dark (controlled by an automatic timer).
- Food:** Agway Purina Guinea Pig Diet, ad libitum.
- Water:** Automatic watering system, ad libitum. Municipal water supply (Elizabethtown Water Company).

V. MATERIALS (cont.)B. Test Animals (cont.):

- Contaminants:** There were no known contaminants reasonably expected to be found in food or water which would interfere with the results of this study.
- Animal Identification:** Each animal was identified with a metal ear tag, bearing a unique animal number, prior to testing.
- Selection:** Animals were randomly placed in cages upon receipt, and were placed on study as available at the time of study initiation. Any animals considered unsuitable because of poor health, outlying body weights, or unacceptable skin were excluded.

VI. METHODSA. Route of Administration:

- Induction:** Intradermal injection, in the clipped shoulder region.  
Topical application, on the clipped shoulder region.
- Challenges:** Topical application, on the clipped skin of the flanks.

B. Justification for Route of Administration:

The study is intended to provide information on the health hazards likely to arise from exposure to the test material by the dermal route; skin contact is a possible worker and consumer exposure route. The guinea pig maximization test is an acceptable method for evaluating test materials suspected of being potential dermal sensitizers.

C. Range-Finding Study: (Results presented in Appendix A)1. Intradermal

To confirm that the concentration proposed for intradermal injection (5.0%) did not produce extensive necrosis or ulceration or severe systemic toxicity, two animals were administered intradermal injections (2 sites per animal) of a 5.0% v/v concentration of the test material in distilled water. Injections of 0.1 ml per site were made intradermally using a 1.0 cc syringe and a 26 gauge 5/8" needle. Observations were made at 24 and 48 hours for necrosis and ulceration. Results, presented in Appendix A, indicated that a 5.0% concentration produced only local necrosis (i.e., no extensive necrosis or ulceration occurred). Therefore, this concentration was used for the intradermal induction administration.

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VI. METHODS (cont.)C. Range-Finding Study (cont.):2. Topical

A topical range-finding study was performed as follows to determine the highest concentration which produced mild irritation (to be used for induction) and the highest concentration which did not produce irritation (to be used for challenge). Four concentrations were administered initially (to six animals; four sites per animal).

<u>Number of Animals</u>	<u>Concentrations</u>
6 (3 per sex)	10, 25 and 50% v/v; 100%

Vehicle: Distilled water

Preparation of Animals:

The animals were closely clipped on the dorsal and lateral surfaces with an electric clipper. Each animal was dosed at four different sites (one concentration, twice), two on either side of the spinal column.

Application of Test Material:

Each test material mixture was applied to saturation, to a 2x2 cm square of filter paper, which was then placed directly on the test site. The sites were then covered with plastic sheeting which was secured by wrapping the torso of each animal with an elastic adhesive bandage (Elastoplast®). After 24 hours the bandages, sheeting and patches were removed.

Observations:

Observations for signs of dermal irritation (erythema, edema and eschar formation) were made approximately 24, and 48 hours after removal of the patches. At each observation, all treated sites were scored for erythema, edema and eschar formation using the scoring system in Appendix B.

Results, Selection of Doses:

Based on results of this study, the following concentrations were selected:

Induction: 50%  
Challenge: 25%

VI. METHODS (cont.)D. Preparation of Test and Control Materials:1. Induction (Intradermal):Site One:

Adjuvant: 5 ml of FCA was added to 5 ml deionized water, to produce a 0.5 ml/ml (50% v/v) mixture.

Site Two:

Test Material: 0.5 ml of AEEA was added to 9.5 ml of distilled water and mixed to produce a 0.05 ml/ml (5% v/v) mixture.

Site Three:

Test Material: 0.5 ml of AEEA was added to 9.5 ml of distilled water and mixed to produce a 0.05 ml/ml (5% v/v) mixture.

2. Topical Application, Induction and Challenge:Test Materials:

Induction: 5.0 ml of AEEA was added to 5.0 ml of distilled water to produce a 0.50 ml/ml (50% v/v) mixture.

Challenge: 2.5 ml of AEEA was added to 7.5 ml of distilled water to produce a 0.25 ml/ml (25% v/v) mixture.

Cross-Challenge: Aqueous mixtures of appropriate concentrations of AEEA and the other materials were prepared in the same manner as challenge.

3. Frequency of Preparation:

Fresh mixtures were prepared prior to each administration.

VI. METHODS (cont.)E. Dosing Procedure:1. Induction Phase - Intradermal Injection (Day 0):

On the day prior to the injections, the hair in the shoulder region (approximately 4x6 cm) was clipped short with an electric clipper. Substances were then administered by intradermal injection, using a 1.0 cc syringe and a 25 gauge 5/8" needle, in the clipped shoulder area. One row of three injections was made on each side, for a total of six injections. The injections consisted of the following:

- 1) Two sites with 0.1 ml of FCA/water emulsion per site.
- 2) Two sites with 0.1 ml of test material or vehicle per site.
- 3) Two sites with 0.1 ml of test material or vehicle/FCA emulsion per site.

Injections 1) and 2) were given close together and nearest to the head; injection 3) was given more caudally.

2. Induction Phase - Topical Application (Day 7):a. Preparation of Animals:

The hair in the shoulder area was re-clipped on the day prior to topical application.

b. Administration:

The test material was applied to a 2x4 cm filter paper to saturation (0.2 ml of material). The filter paper was then placed on the test site and secured with tape. This was then covered by overlapping impermeable plastic, which was firmly secured by an elastic adhesive bandage which was wound around the torso of the animal. The patches were left in place for 48 hours after which they were removed and the skin wiped free of any excess material.

3. Challenge Phase (Day 21):a. Test Animals:

The hair was removed from a 5x5 cm area on the right flank, by clipping as described previously, on the day prior to the challenge application. Patches were applied to the flank using the same procedure as for topical application on Day 7, except that a 2x2 cm piece of filter paper was used and allowed to remain on the animal for 24 hours. Dermal readings were made on all animals 24 and 48 hours after the removal of the patches. The challenge area was gently clipped after the 24 hour observation.

VI. METHODS (cont.)E. Dosing Procedure (cont.):3. Challenge Phase (Day 21) (cont.):b. Irritation Control Animals:

In order to differentiate animal reactions produced by irritation from those produced by sensitization, previously untreated animals were subjected to the same challenge procedure as the animals which received the induction exposures.

4. Cross-Challenge (Day 28):

Seven days after the challenge exposure, the cross-challenge treatment was administered. Animals were clipped as before and the test material was administered in a similar manner as in the challenge phase but at a previously untreated site (left flank). Smaller patches (S/P Adhesive Bandages - 7/8 square inches) were used in order to allow all of the materials to fit on the test site. Materials were applied to saturation (0.03 ml per patch). After twenty-four hours of exposure, the patches were removed and the skin wiped free of any excess test material.

VII. EXPERIMENTAL EVALUATIONA. Viability Check:

Twice daily

B. Body Weights:

Pretest (day prior to first induction)  
Termination (3 days after the first challenge)

C. In-Life Observations:

Weekly

D. Dermal Observations:

Intervals: 24 and 48 hours after removal of patches applied at challenge and cross-challenge.

Methods: Dermal responses were scored according to the scale presented in Appendix B.

VIII. RAW DATA

All raw data and the original study protocol and final report will be retained in the Bio/dynamics Inc. Archives.

**IX. RESULTS AND DISCUSSION****A. Mortality**

All animals survived throughout the study.

**B. Body Weights (Table I)**

All animals gained weight during the study.

**C. Dermal Responses****1. Challenge**

A summary of dermal responses is presented in Table II.

Individual dermal observations are presented in Table III. Redness or edema at the challenge site at any of the observations which is greater than that seen in the irritation control animals is considered an allergic response. In general, dermal scores of 1 or greater (in the absence of dermal response in irritation control animals) are considered clearly indicative of sensitization. Scores of 0.5 (barely perceptible erythema) are considered equivocal, although a high percentage of scores of 0.5 in treated animals with no dermal response in irritation control animals is considered suggestive of sensitization. Number (percentages) of animals reacting, rather than intensity of reactions, is the criterion for categorizing materials as sensitizers and assessing sensitization potency. Allergenicity categories are presented in Appendix B.

Eight of the twenty animals challenged with Aminoethylethanolamine (AEEA) (Group IA) exhibited clear dermal responses (scores of 1 or higher) 24 and/or 48 hours after challenge; six additional animals exhibited scores of 0.5 at one or both intervals. Based on clear responses in eight of the twenty animals (40%), AEEA would be considered to be a moderate dermal sensitizer under conditions of this study. No dermal responses occurred in any of the ten irritation control animals (Group IB).

IX. RESULTS AND DISCUSSION (cont.)C. Dermal Responses (cont.):

## 2. Cross-Challenge

A summary of dermal responses at cross-challenge is presented in Table IV; individual scores are presented in Table V. Positive responses (scores of 1 or higher at 24 and/or 48 hours after test material application) occurred as follows:

<u>Material</u>	<u>Group IA</u> (Test Animals)	<u>Group IC</u> (Irritation Controls)
EDA	3/20	0/10
DETA-HP	7/20	2/10
TETA	7/20	2/10
AEP	9/20	6/10
TEPA	2/20	4/10
Piperazine	1/20	0/10

Based on these responses, cross-sensitization to EDA, DETA-HP and TETA was apparent and cross-sensitization to Piperazine was suggested. Although minimal responses to DETA-HP and TETA were seen in irritation controls, responses in test animals clearly exceeded those in controls. A clear response in one of the twenty Piperazine-treated animals and a possible slight response (score of 0.5) in two others, in the absence of significant irritation in control animals (one animal with a score of 0.5), suggests that some cross-sensitization to this material may have occurred. No cross-sensitization to AEP or TEPA was apparent. Responses in test material treated animals were similar to or less pronounced than those seen in irritation control animals.

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5502-89**X. CONCLUSION**

Under conditions of this study, Aminoethylethanolamine (AEEA) exhibited a moderate potential to produce dermal sensitization in the guinea pig and induced cross-sensitization to Ethylenediamine-UHP (EDA), Diethylenetriamine (DETA-HP), Triethylenetetramine (TETA). Possible slight cross-sensitization to Piperazine was also suggested.

Carol S. Auletta  
Carol S. Auletta, B.A., D.A.B.T.  
Associate Director of Toxicology

7/11/90  
Date

Ira W. Daly  
Ira W. Daly, Ph.D., D.A.B.T.  
Senior Vice President  
Director of Toxicology

7/11/90  
Date

TABLE I  
GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)  
BODY WEIGHTS (GRAMS)  
PRETEST AND TERMINATION

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	<u>Animal No. and Sex</u>	<u>Pretest</u>	<u>Termination</u>
Group IA AEEA	3027 M	333	461
	3028 M	400	577
	3029 M	357	528
	3030 M	386	562
	3031 M	386	470
	3032 M	324	433
	3033 M	394	504
	3034 M	354	470
	3035 M	364	530
	3036 M	379	491
	3184 F	339	430
	3088 F	339	362
	3186 F	309	385
	3187 F	313	409
	3188 F	306	412
	3189 F	314	382
	3219 F	345	463
	3191 F	319	430
	3220 F	325	339
3193 F	334	397	

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M=Male; F=Female.

TABLE I (cont.)

GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)

BODY WEIGHTS (GRAMS)

PRETEST AND TERMINATION

---

	<u>Animal No. and Sex</u>	<u>Pretest</u>	<u>Termination</u>
Group IB Challenge Irritation Controls	3042 M	392	479
	3043 M	368	507
	3044 M	417	607
	3045 M	393	557
	3046 M	340	462
	3199 F	303	382
	3200 F	312	370
	3103 F	297	376
	3202 F	302	431
	3095 F	339	443
Group IC Cross- Challenge Controls	3047 M	347	491
	3048 M	375	529
	3049 M	356	469
	3050 M	403	494
	3051 M	353	493
	3204 F	311	401
	3205 F	336	448
	3206 F	386	506
	3207 F	322	432
	3208 F	322	455

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M=Male; F=Female.

TABLE II  
GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)  
INCIDENCE OF DERMAL RESPONSE AT CHALLENGE

Group	Material	Conc.	Hr:	Dermal Scores <sup>a</sup>								Total No. of Animals	
				0	0.5	1	2	3	Ed	N	E		S
IA	AEEA	25%	24	11	4	5	0	0	0	0	0	0	20
			48	7	5	6	2	0	0	0	0	0	20
IB	AEEA (Irritation Control) <sup>b</sup>	25%	24	10	0	0	0	0	0	0	0	0	10
			48	10	0	0	0	0	0	0	0	0	10

<sup>a</sup>Scored using the scale presented in Appendix B.

<sup>b</sup>Irritation control group was treated at challenge only.

Ed=Edema; N=Necrosis; S=Superficial or Focal Necrosis; E=Eschar.

TABLE III  
GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)  
INDIVIDUAL DERMAL SCORES<sup>a</sup> AT CHALLENGE  
GROUP IA: 25% AEEA (Animals Treated During Induction)

Males			Females		
Animal No. and Sex	Interval		Animal No. and Sex	Interval	
	24 Hours	48 Hours		24 Hours	48 Hours
3027 M	0	0.5	3184 F	0.5	0.5
3028 M	0	0.5	3088 F	0	0
3029 M	0	0	3186 F	0	0
3030 M	1	1	3187 F	0	0.5
3031 M	1	2	3188 F	1	1
3032 M	0	0.5	3189 F	0	1
3033 M	0	0	3219 F	0	0
3034 M	0.5	0	3191 F	1	1
3035 M	0	0	3220 F	0.5	1
3036 M	1	2	3193 F	0.5	1

<sup>a</sup>Scored using scale presented in Appendix B.  
M=Male; F=Female.

TABLE III (cont.)  
GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)  
INDIVIDUAL DERMAL SCORES<sup>a</sup> AT CHALLENGE  
GROUP IB: 25% AEEA (Irritation Control Animals)

<u>Animal No. and Sex</u>	<u>Interval</u>	
	<u>24 Hours</u>	<u>48 Hours</u>
3042 M	0	0
3043 M	0	0
3044 M	0	0
3045 M	0	0
3046 M	0	0
3199 F	0	0
3200 F	0	0
3103 F	0	0
3202 F	0	0
3095 F	0	0

<sup>a</sup>Scored using scale presented in  
Appendix B.  
M=Male; F=Female.

TABLE IV  
GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEFA)  
INCIDENCE OF DERMAL RESPONSE AT CROSS-CHALLENGE

Group	Material	Conc.	Hr:	Dermal Scores <sup>a</sup>										Total No. of Animals
				0	0.5	1	2	3	Ed	N	E	S		
IA	EDA	5%	24	14	4	2	0	0	0	0	0	0	0	20
			48	17	0	3	0	0	0	0	0	0	0	20
IC	EDA (Irritation Control) <sup>b</sup>	5%	24	10	0	0	0	0	0	0	0	0	0	10
			48	10	0	0	0	0	0	0	0	0	0	10
IA	DETA HP	25%	24	11	2	4	2	1	0	1	0	2	20	
			48	15	1	2	0	2	0	2	1	1	20	
IC	DETA HP (Irritation Control) <sup>b</sup>	25%	24	8	0	2	0	0	0	0	0	0	10	
			48	8	1	1	0	0	0	0	0	1	10	
IA	TETA	50%	24	12	3	3	2	0	0	0	0	1	20	
			48	15	1	3	1	0	0	0	0	0	20	
IC	TETA (Irritation Control) <sup>b</sup>	50%	24	8	0	2	0	0	0	0	0	0	10	
			48	9	0	1	0	0	0	0	0	1	10	
IA	AEP	25%	24	9	5	4	1	1(0) <sup>c</sup>	0	1(0) <sup>c</sup>	0	0	20	
			48	10	3	6	1	0	0	0	0	0	20	
IC	AEP (Irritation Control) <sup>b</sup>	25%	24	4	1	3	2	0	0	0	0	0	10	
			48	4	3	2	0	1	2	1	0	0	10	
IA	TEPA	50%	24	19	1	0	0	0	0	0	0	0	20	
			48	18	0	2	0	0	0	0	0	0	20	
IC	TEPA (Irritation Control) <sup>b</sup>	50%	24	6	1	2	1	0	0	0	0	1	10	
			48	8	1	1	0	0	0	0	0	0	10	
IA	Piperazine	25%	24	17	2	0	0	1	0	1	0	0	20	
			48	19	0	0	0	1	0	1	0	0	20	
IC	Piperazine (Irritation Control) <sup>b</sup>	25%	24	10	0	0	0	0	0	0	0	0	10	
			24	9	1	0	0	0	0	0	0	0	10	

<sup>a</sup>Scored using the scale presented in Appendix B.

<sup>b</sup>Irritation control groups were treated at cross-challenge only.

<sup>c</sup>Some scores considered questionable (see individual data); number of scores considered definitive is presented in parentheses.

Ed=Edema; N=Necrosis; E=Eschar; S=Superficial or Focal Necrosis.

TABLE V  
GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)  
INDIVIDUAL DERMAL SCORES<sup>a</sup> AT CROSS-CHALLENGE  
GROUP IA: 25% AEEA<sup>b</sup>

Animal No. and Sex	EDA - 5%		DETA-HP - 25%		TETA - 50%	
	24 Hours	48 Hours	24 Hours	48 Hours	24 Hours	48 Hours
3027 M	0	0	0	0	0	0
3028 M	0	0	0	0	0	0
3029 M	0	0	1 <sup>c</sup>	1	0	0
3030 M	1	1	1 <sup>c</sup>	1	0.5	1
3031 M	0.5	1	0	0	2 <sup>c</sup>	2
3032 M	0	0	0	0	0	0
3033 M	0	0	0	0	0	0
3034 M	0	0	0	0	2	1
3035 M	0	0	2	0	0	0
3036 M	0	0	0	0	0	0
3184 F	0	0	0	0	1	0
3088 F	0	0	0.5	0.5	0	0
3186 F	0	0	1	0	1	0
3187 F	0	0	0	0	0	0
3188 F	0	0	3,N	3,N,E	0	0
3189 F	0.5	0	2	3,N,S	0	0
3219 F	0.5 <sup>f</sup>	0	0	0	0	0.5
3191 F	1	1,D	1	0	0.5	0
3220 F	0.5	0	0	0	0.5	1
3193 F	0	0	0.5	0	1	0

<sup>a</sup>Scored using scale presented in Appendix B.

<sup>b</sup>Group IA received 50% AEEA during induction.

<sup>c</sup>Foci of necrosis.

M=Male; F=Female; N=Necrosis; E=Eschar; S=Superficial Necrosis; D=Desquamation.

TABLE V (cont.)

GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)

INDIVIDUAL DERMAL SCORES<sup>a</sup> AT CROSS-CHALLENGE

GROUP IA: 25% AEEA<sup>b</sup>

Animal No. and Sex	AEP - 25%		TEPA - 50%		Piperazine - 25%	
	24 Hours	48 Hours	24 Hours	48 Hours	24 Hours	48 Hours
3027 M	0	0	0	0	0	0
3028 M	0.5	0.5	0	0	0	0
3029 M	0	0	0	0	0	0
3030 M	1	1	0	1	0	0
3031 M	0.5	1	0	0	0	0
3032 M	2	1	0	0	0	0
3033 M	1	1	0	0	0	0
3034 M	0.5	1	0	0	0	0
3035 M	1	0	0	0	0	0
3036 M	0	0	0	0	0	0
3184 F	(3,N)	1,D <sup>d</sup>	0	0	0	0
3088 F	0	0	0	0	0	0
3186 F	0	0	0	0	3,N	3,N
3187 F	0.5	0	0	0	0	0
3188 F	0	0	0	0	0	0
3189 F	1	0.5	0	0	0	0
3219 F	0	0.5	0	0	0	0
3191 F	0.5	0	0.5	1	0.5	0
3220 F	0	0	0	0	0	0
3193 F	0	2,D	0	0	0.5	0

<sup>a</sup>Scored using scale presented in Appendix B.

<sup>b</sup>Group IA received 50% AEEA during induction.

<sup>d</sup>The 48-hour observation was confirmed, i.e., no significant irritation at 48 hours; apparent severe irritation at 24 hours suggests that observations at 24 hours were due to dosing procedure (irritation from tape/patch removal, etc.) rather than a true response to the test material. Questionable scores are presented in parentheses.

M=Male; F=Female; N=Necrosis; D=Desquamation.

TABLE V (cont.)

GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)

INDIVIDUAL DERMAL SCORES<sup>a</sup> AT CROSS-CHALLENGE CONTROLS

GROUP IC: 25% AEEA<sup>e</sup>

Animal No. and Sex	EDA - 5%		DETA-HP - 25%		TETA - 50%	
	24 Hours	48 Hours	24 Hours	48 Hours	24 Hours	48 Hours
3047 M	0	0	1	0	0	0
3048 M	0	0	0	0	0	0
3049 M	0	0	0	0	0	0
3050 M	0	0	1	1 <sup>c</sup>	0	0
3051 M	0	0	0	0	0	0
3204 F	0	0	0	0	0	0
3205 F	0	0	0	0	0	0
3206 F	0	0	0	0	1	0
3207 F	0	0	0	0	0	0
3208 F	0	0	0	0.5	1	1 <sup>c</sup>

<sup>a</sup>Scored using scale presented in Appendix B.

<sup>c</sup>Foci of necrosis.

<sup>e</sup>Group IC=Irritation control.

M=Male; F=Female; N=Necrosis; Ed=Edema.

TABLE V (cont.)

GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)

INDIVIDUAL DERMAL SCORES<sup>a</sup> AT CROSS-CHALLENGE CONTROLS

GROUP IC: 25% AEEA<sup>e</sup>

Animal No. and Sex	AEP - 25%		TEPA - 50%		Piperazine - 25%	
	24 Hours	48 Hours	24 Hours	48 Hours	24 Hours	48 Hours
3047 M	1	0.5	1	0	0	0
3048 M	2	0	2	0.5	0	0
3049 M	0.5	0.5	0	0	0	0
3050 M	1	0.5	1	0	0	0.5
3051 M	1	3,N	0	0	0	0
3204 F	0	0	0	0	0	0
3205 F	0	1,Ed	0	0	0	0
3206 F	2	1,Ed	0	0	0	0
3207 F	0	0	0.5 <sup>c</sup>	1	0	0
3208 F	0	0	0	0	0	0

<sup>a</sup>Scored using scale presented in Appendix B.

<sup>c</sup>Foci of necrosis.

<sup>e</sup>Group IC=Irritation control.

M=Male; F=Female.

APPENDIX A

GUINEA PIG MAXIMIZATION STUDY WITH Aminoethylethanolamine (AEEA)

RANGE-FINDING STUDY

INTRADERMAL INJECTIONS:<sup>a</sup>

Animal No. and Sex	Site #1 (5.0%) <sup>b</sup>		Site #2 (5.0%) <sup>b</sup>	
	24 Hr	48 Hr	24 Hr	48 Hr
3008 M	N+	N+	N+	N+
3114 F	N+	N+	N+	N+

TOPICAL APPLICATION:<sup>c</sup>

Animal No. and Sex	Concentration							
	100%		50% <sup>b</sup>		25% <sup>b</sup>		10% <sup>b</sup>	
	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr	24 Hr	48 Hr
2947 M	0.5	0.5,Ed	0	0	0	0	0	0
2952 M	3,N	3,N,Ed	2	0.5,Ed	0	0	0	0
2976 M	2	1,Ed	0	0	0	0	0	0
3129 F	0	0	0	0	0	0	0	0
3130 F	0.5	0	0	0	0	0	0	0
3131 F	0.5	0.5	0.5	0	0	0	0	0

<sup>a</sup>Observed for necrosis and ulceration only:

- 0=No necrosis or ulceration
- N+=Local necrosis (acceptable)
- N++=Extensive necrosis (not acceptable)
- U=Ulceration (not acceptable)

<sup>b</sup>Vehicle: distilled water.

<sup>c</sup>Scored according to scale presented in Appendix B.  
M=Male; F=Female; N=Necrosis; Ed=Edema.

APPENDIX B

1. EVALUATION OF DERMAL RESPONSE

Evaluation of Dermal Response

No reaction.....	0
Very slight (barely perceptible) erythema, usually nonconfluent.....	0.5
Slight (well-defined) erythema, usually confluent.....	1
Moderate erythema.....	2
Severe erythema, with or without edema, necrosis or eschar formation.....	3

If edema, necrosis or eschar formation occurred, they were indicated using the following code:

Edema.....	Ed
Necrosis.....	N
Eschar.....	E
Superficial Necrosis.....	S

2. ALLERGENICITY RATING

<u>Sensitization Rate (%)</u>	<u>Grade</u>	<u>Classification</u>
1 - 8	I	Weak
9 - 28	II	Mild
29 - 64	III	Moderate
65 - 80	IV	Strong
81 - 100	V	Extreme

Appendix C

Historical Control Data

Sensitization of Guinea Pigs to Dinitrochlorobenzene

<u>Study No.</u>	<u>Dates of Study</u>	<u>DNCB Concentration<sup>a</sup> Induction Challenge</u>	<u>No. of Inductions</u>	<u>Number Sensitized<sup>b</sup></u>	<u>% Sensitized</u>
8.	8/30/88-9/29/88	0.5% 0.3%	3	10/10	100%
9.	8/31/88-10/7/88	0.5% 0.3%	3	9/9 <sup>c</sup>	100%
10.	11/2/88-12/2/88	0.5% 0.3%	3	10/10	100%
11.	3/22/89-4/28/89	0.5% 0.3%	3	10/10 <sup>d</sup>	100%
12.	5/17/89-6/16/89	0.5% 0.3%	3	10/10 <sup>e</sup>	100%
13.	1/25/89-2/24/89	0.5% 0.3%	3	10/10	100%
14.	7/26/89-9/01/89	0.5% 0.3%	3	10/10	100%

<sup>a</sup>Vehicle: Induction=80% ethanol; Challenge=acetone.

<sup>b</sup>Animals were considered sensitized if they exhibited a dermal score of 1 or greater. Irritation controls exhibited scores of 0 or 0.5 (±) unless otherwise noted.

<sup>c</sup>One animal died during study and one animal in irritation control group exhibited a score of 1 at 48 hours.

<sup>d</sup>One animal in irritation control group exhibited a score of 1 at 24 hours.

<sup>e</sup>Two animals in irritation control group exhibited a score of 1 at 24 and/or 48 hours.

Appendix D

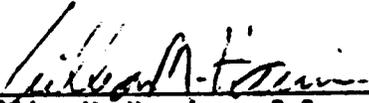
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Quality Assurance Statement

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Listed below are dates that this study was inspected by the Quality Assurance Unit of Bio/dynamics, Inc. and the dates findings were reported to the Study Director and Management.

<u>Dates of Inspection</u>	<u>Reported to Study Director</u>	<u>Reported to Management</u>
10/19/89 4/8-12/90 and 4/25/90	10/26/89 5/10/90	12/1/89 and 12/19/89 5/10/90 and 5/30/90

  
\_\_\_\_\_  
William M. Harrison, B.S.  
Manager, Quality Assurance

  
\_\_\_\_\_  
Date

Appendix E

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Compliance Statement

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To the best of our knowledge, the study (Bio/dynamics Project No.: 5502-89), was conducted in general conformance with the Good Laboratory Practice Standards of the Environmental Protection Agency TSCA, 40 CFR Part 792 with the following exceptions:

Test substance characterization and stability data remains the responsibility of the sponsor. Assay to verify concentration, stability and homogeneity of the test substance in the carrier were not performed.

These deviations should not affect the results or conclusions of the study.

Carol S. Auletta  
Carol S. Auletta, B.A., D.A.B.T.  
Study Director  
Associate Director of Toxicology

7/11/90  
Date

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**CERTIFICATE OF AUTHENTICITY**

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