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TSCA Section 8(e) Notification on:
Boric acid, C_{13-rich}, C₁₁₋₁₄ isoalkyl pentyl esters
[Document Control Number: 8EHQ-97-14085]

Dear Sir/Madame:

Pursuant to our TSCA 8(e) submission [Document Control Number: 8EHQ-97-14085] on the skin sensitization potential of a Boric acid, C_{13-rich}, C₁₁₋₁₄ isoalkyl pentyl esters [Chemical Abstract Number (166747-78-6)], we are providing a copy of the final guinea pig maximization report for your records.

Should be 167 747 - 78 - 6

Confidentiality is being claimed for the company name, names of company employees, chemical identities, and trade names. All pages containing this information have been stamped "Confidential". Two copies of the supplemental information are being submitted, the confidential information has been circled in one copy and excised from the other. The latter is intended for the EPA's Public File.

Sincerely,

This report is being made in compliance with Section 8(e) of the Toxic Substances Control Act (15 U.S.C. 2607), pursuant to our understanding of the Statement of Interpretation and Enforcement Policy (43 Fed. Reg. 11110 et seq.). It has been compiled based on information available within the time period given. While we believe the tests reported were properly performed, no representation can be made as to their accuracy of content. The corporation and individual signator also reserve the right to supplement any or all of the data contained herein and to revise or amend any conclusion drawn therefrom.

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Huntingdon
Life Sciences

STUDY NO.: 97-1691

GUINEA PIG MAXIMIZATION TEST
(Method of Magnusson and Kligman)

Final Report

Author: Diann L. Blanset, M.S., D.A.B.T.

Performed by: Huntingdon Life Sciences
P.O. Box 2360, Mettlers Road
East Millstone, New Jersey 08875-2360

Submitted to:

Attn:

Date: 20 January 1998

Page 1 of 33

GUINEA PIG MAXIMIZATION TEST
(Method of Magnusson and Kligman)

ABSTRACT

This study was conducted for Mobil Business Resources Corporation in order to evaluate the allergic contact sensitization potential of in guinea pigs. Data from this study may serve as a basis for classification and labelling of the test material. This study was performed at Huntingdon Life Sciences, P.O. Box 2360, Mettlers Road, East Millstone, New Jersey 08875-2360. Dosing was initiated on 7 October 1997 and observations were completed on 31 October 1997.

The procedures used are 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, Vol. 52, pp 268-276 and in Allergic Contact Dermatitis in the Guinea Pig: Identification of Contact Allergens, Thomas, Springfield, IL, 1970. The test material was administered at 5% concentration for the intradermal Induction, and undiluted for the topical Induction, to 10 male Dunkin Hartley guinea pigs. Fourteen days after the last induction exposure, the Challenge treatment was administered topically to two separate sites at 100% and 50% concentrations. In order to differentiate dermal reactions produced by irritation from those produced by sensitization, 5 males (treated concurrently during Induction with only vehicle and FCA/water emulsion) were subjected to the same Challenge procedures as the animals which received test material during the Induction exposures.

Observations for mortality were made twice daily. Body weights were measured pretest and three days after Challenge. Animals were also observed prior to treatment and weekly during the study for general health. During the Induction phase, dermal evaluations were made approximately 24 hours after injection or removal of patches. In addition, dermal evaluations were made approximately 24 and 48 hours after removal of the patches during the Challenge Phase.

All animals survived and gained weight throughout the study.

Responses seen during the induction phase were typical of responses seen in this study design and are probably due to administration of FCA.

Five of the ten animals challenged with neat test material exhibited clear dermal responses (scores of 1 or greater) and the remaining five animals exhibited scores of less than 1. Four of the test animals also exhibited edema. One irritation control animal exhibited a clear dermal response (score of 1) and the remaining four irritation control animals were free of dermal responses. The Incidence Index of Sensitization to the test material at Challenge was 50%. The Severity Indices for the test group at 24 and 48 hours were both 0.5. For the irritation control groups

at 24 and 48 hours; the Indices were 0.0 and 0.2, respectively.

Seven of ten animals challenged with a 50% concentration of exhibited clear dermal responses (scores of 1 or greater) and the remaining three animals exhibited scores of less than 1. All five irritation control animals were free of significant dermal responses. The Incidence Index of Sensitization to a 50% concentration of the test material at Challenge was 70%. The Severity Indices for the test group at 24 and 48 hours were 0.7 and 0.9, respectively, and for the irritation control groups at 24 and 48 hours were 0.1 and 0.2, respectively.

Under conditions of this study, exhibited a potential to produce dermal sensitization in guinea pigs and would be classified as a strong sensitizer and be considered a risk phrase R43.

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I. INTRODUCTION

This study was conducted for order to evaluate the allergic contact sensitization potential of in guinea pigs. This study was performed at Huntingdon Life Sciences, P.O. Box 2360, Mettlers Road, East Millstone, New Jersey 08875-2360. The procedures used are 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, Vol. 52, pp 268-276 and in Allergic Contact Dermatitis in the Guinea Pig: Identification of Contact Allergens, Thomas, Springfield, IL, 1970.

The procedures used followed the methods described in:

OECD (Organization for Economic Cooperation and Development): Guidelines for Testing of Chemicals, July 17, 1992, (No. 406).

EEC (European Economic Community): Methods for the Determination of Toxicity, Annex to Directive 92/69/EEC (OJ No. L383A, 29.12.92), Part B, Method B.6. Skin Sensitization.

This report has been reviewed by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, to assure its conformance with the protocol and the raw data. All raw data, the original study protocol, a sample of the vehicles and test material and the final report will be retained on file in the archives of the Testing Facility.

II. EXPERIMENTAL DESIGN

Group	Test Material	Number of Animals	Concentration (%)				
			Induction			Challenge	
			Intradermal			Topical ^d	Topical
			Site 1	Site 2	Site 3		
1		10 M	a	5 ^b	5 ^c	100	100/50 ^b
2	(Irritation Control)	5 M	a	e	f	e	100/50 ^b

^a50% FCA/water emulsion administered.
^bVehicle: propylene glycol.
^cVehicle: 50% FCA/water emulsion.
^dAnimals were pretreated with 10% sodium laurel sulfate.
^e100% propylene glycol administered.
^fDosed with 50% propylene glycol in 50% FCA/water emulsion.
M=Male.

III. DATES OF STUDY

Study Initiation: 11 September 1997
(Date Study Director signed the protocol)

Animal Receipt:
Range-Finding:
Intradermal: 22 September 1997
Topical: 28 July 1997
Sensitization: 22 September 1997

Range-Finding:
Intradermal: 30 September 1997 - 2 October 1997
Topical: 16 September 1997 - 19 September 1997

Initiation of Dosing: 7 October 1997
(Experimental Start)

Last In-Life Evaluation: 31 October 1997
(Experimental termination date)

Study Completion: 20 January 1998
(Date Study Director signed the final report)

IV. STUDY PERSONNEL

Study Director: Diann L. Blanset, M.S., D.A.B.T.

Study Supervisor: Jill DeSiato

Study Monitor: Christine Cimpko, B.S.
(Report Preparation)

V. MATERIALS

- A. Test Animals: Albino Guinea Pigs**
1. Stock: Dunkin Hartley Haz:(DH)FBR
 2. Supplier: Covance Research Products Inc., Denver, Pennsylvania

V. MATERIALS (cont.)

A. Test Animals (cont.):

3. Justification for Test System Selection:

Standard laboratory animal for dermal sensitization studies. The Dunkin Hartley albino guinea pig was used because of its availability and because of the existing historical data base for comparative evaluation.

Huntingdon Life Sciences has a historical base of data for animals from the same source as those used in this study demonstrating susceptibility to dermal sensitization with a known sensitizer, hexylcinnamic aldehyde (HCA), when tested using this protocol. Groups of animals are tested with this positive control material periodically (approximately every four to six months) to demonstrate continuing susceptibility to sensitization. Historical positive control data is presented in Appendix C.

4. Animal Requirements/Specifications:

a. Number of Animals:

- (1) Range-finding: 6 males
- (2) Sensitization Study: 10 males
- (3) Irritation Controls: 5 males

b. Age:

Range-finding:

Intradermal: Approximately 4-7 weeks at dosing.
Topical: Approximately 9-12 weeks at dosing.

Sensitization Study: Approximately 5-7 weeks at first dose.

c. Weight Range (Sensitization and Irritation Control Animals):

396 - 485 grams

V. MATERIALS (cont.)

A. Test Animals (cont.):

5. Acclimation Period:

Range-finding Animals: 8 or 50 days
Sensitization Animals: 15 days

Observations: All animals were checked for viability twice daily. Prior to assignment to study all animals received a physical examination to ascertain suitability for study.

6. Animal Husbandry:

Currently acceptable practices of good animal husbandry were followed, e.g., Guide for the Care and Use of Laboratory Animals; National Academy Press; 1996. Huntingdon Life Sciences, East Millstone, New Jersey, is fully accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC).

- a. Housing: Individually housed in suspended, stainless steel cages with wire mesh bottoms.
- b. Food: Certified Guinea Pig Diet, No. 5026; (PMI Feeds, Inc., St. Louis, MO) *ad libitum*.
- c. Feed Analysis: Analysis of each feed lot used during this study was performed by PMI Feeds, Inc. Results are maintained on file at the Testing Facility.
- d. Water: Automatic watering system, *ad libitum*. Municipal water supply (Elizabethtown Water Company, Westfield, New Jersey).
- e. Water Analysis: Monthly analysis of water supplied to the Testing Facility was provided by Elizabethtown Water Company, Westfield, New Jersey (Raritan-East Millstone Plant). Results are maintained on file at the Testing Facility.

Biannual chemical and microbiological analyses of water samples collected from representative rooms in the Testing Facility were conducted to assure that water met standards specified under the EPA National Primary Drinking Water Regulations (40 CFR Part 141). Results are maintained on file at the Testing Facility.

V. MATERIALS (cont.)

A. Test Animals (cont.):

6. Animal Husbandry (cont.):

f. **Contaminants:** There were no known contaminants reasonably expected to be found in food or water which would interfere with the results of this study.

g. **Veterinary Care:** Animals were monitored by the technical staff for any conditions requiring possible veterinary care.

h. 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).

7. Selection for Study:

More animals than required for the study were purchased and equilibrated. Animals were arbitrarily placed in cages upon receipt, and were placed on study as available at the time of study initiation. Animals considered unsuitable on the basis of pretest physical examinations, outlying body weights, or unacceptable skin were excluded. Disposition of all animals not utilized in the study is maintained on file at the Testing Facility.

8. Identification:

Each animal was identified with a Monel ear tag, bearing a unique animal number, prior to testing. Each cage was provided with a cage card which contained the study number, animal number, sex and dose-group information.

B. Test Material:

Lot/Batch No.:

Description:

Golden yellow liquid; mild alcohol odor

Purity:

Assume 100%

Date of Receipt:

8 September 1997

Expiration Date:

27 August 2002

V. MATERIALS (cont.)

B. Test Material (cont.):

Received from:

Storage:

Room temperature

Sampling:

An archival sample of approximately 2 grams is stored in the archives of the Testing Facility.

Analysis:

The identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of the test material remain the responsibility of the Sponsor.

C. Vehicles:

Propylene glycol

Lot Number:

G48608

Description:

Clear, slightly viscous liquid

Purity:

100% as supplied

Date of Receipt:

1 July 1994

Expiration Date:

December 1998

Supplier:

JT Baker Chemical Co.,
Phillipsburg, New Jersey

Storage:

Ambient

Sampling:

An archival sample of approximately 10 grams of each lot number is stored in the archives of the Testing Facility.

Analysis:

The identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of the vehicle remain the responsibility of the Manufacturer.

D. Adjuvant:

1. Adjuvant:

Freund's Complete Adjuvant (FCA)

Lot/Batch No.:

86321LA and 109068LA

Description:

Light yellow liquid

Date of Receipt:

28 January 1997/17 July 1997

Expiration Date:

February 1999/March 2000

Supplier:

Difco Laboratories, Detroit, Michigan

Storage:

Room temperature

Sampling:

An archival sample of one vial of each lot number is stored in the archives of the Testing Facility.

V. MATERIALS (cont.)

D. Adjuvant (cont.):

- 2. Adjuvant: Freund's Complete Adjuvant (FCA)
Analysis: The identity, strength, purity, composition, stability and method of synthesis, fabrication and/or derivation of the adjuvant remain the responsibility of the Manufacturer.
- 3. Vehicle: Distilled Water
Source: Prepared at the Testing Facility from tap water supplied by Elizabethtown Water Company, Westfield, New Jersey.
Storage: Room temperature

E. Enhancer:

- 1. Enhancer: Sodium Lauryl Sulfate
Lot Number: 00513BN
Description: White powder
Purity: 98%
Date of Receipt: 13 February 1996
Expiration Date: 13 February 2001
Supplier: Aldrich Chemical Co., Inc.
Milwaukee, Wisconsin
Storage: Room temperature
Sampling: An archival sample of approximately 10 grams is stored in the archives of the Testing Facility.
- 2. Vehicle: Petrolatum
Lot Number: 95403
Description: Translucent paste
Date of Receipt: 16 February 1996
Expiration Date: 16 February 2001
Supplier: Fischer Scientific
Fairlawn, New Jersey
Storage: Room temperature
Sampling: An archival sample of approximately 10 grams is stored in the archives of the Testing Facility.

VI. METHODS

A. 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 the potential of test materials to produce dermal sensitization.

C. Frequency of Administration:

Day 1: Induction of sensitization by intradermal injection.
Day 8: Induction of sensitization by topical administration.
Day 22: Challenge by topical administration.

D. Duration of Study:

25 days

E. Doses:

Range-finding studies for the test material were performed. Based on these studies, doses were selected for Induction and Challenge.

1. Range-Finding Studies: (Results presented in Appendix A)

a. Preparation of Animals:

Approximately one week prior to test material administration, the animals were pre-treated with two intradermal injections of 0.1 mL (per injection) of a 50% FCA/water emulsion (1:1). Prior to test material administration, the animals were closely clipped over the dorsal and lateral surfaces with an electric clipper.

VI. METHODS (cont.)

E. Doses (cont.):

1. Range-Finding Studies (cont.):

b. Intradermal:

To confirm that the concentration proposed for intradermal injection (5%) did not produce extensive tissue damage or severe systemic toxicity, two animals were administered intradermal injections (2 injections/animal) of a 5% v/v concentration of propylene glycol, one on either side of the spinal column. Injections of 0.1 mL per site were made intradermally using a 1.0 cc syringe and a 25 or 26 gauge 5/8" needle. Observations for dermal irritation were made approximately 24 and 48 hours after the injection using the scoring system in Appendix B. Results are presented in Appendix A.

c. Topical:

A topical range-finding study was performed as follows to determine the concentration of test material which produced mild irritation (to be used for Induction) and the highest concentration which did not produce irritation (to be used for Challenge). Each animal was dosed with four different concentrations, at four different sites (one concentration/site), two on either side of the spinal column.

Number of Animals: 4 males (four concentrations per animal)

Vehicle: propylene glycol

Concentrations: 25, 50, and 75% v/v; 100%

Each test material concentration was applied to saturation (0.1 mL of neat material or mixture), 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 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 are presented in Appendix A.

VI. METHODS (cont.)

E. Doses (cont.):

2. Results, Selection of Doses:

Based on results of these studies, concentrations of
were administered as follows:

Intradermal Induction: 5%
Topical Induction: 100%
Challenge: 100% and 50%

F. Administration of Test Material:

1. Induction Phase - Day 1 (Intradermal Injections):

a. Preparation of Animals:

On the day of the injections, the hair in the shoulder region (approximately 4x6 cm) was clipped short with an electric clipper.

b. Preparation of Test/Control Material:

(1) Site 1: FCA/Water Emulsion:

All Groups: The appropriate amount of FCA was added to distilled water to produce a 0.5 mL/mL (50% v/v) mixture.

(2) Site 2: Test Material in Vehicle:

Group 1: The appropriate amount of propylene glycol was added to to produce a 0.05 g/mL (5% w/v) mixture.

Group 2: No preparation was necessary; propylene glycol was administered as received.

(3) Site 3: Test Material in FCA/water Emulsion:

Group 1: The appropriate amounts of distilled water and FCA were added to to produce a 0.05 mL/mL (5% v/v) mixture.

Group 2: The appropriate amounts of distilled water and FCA were added to propylene glycol to produce a 0.5 mL/mL (50% v/v) mixture.

VI. METHODS (cont.)

F. Administration of Test Material (cont.):

1. Induction Phase - Day 1 (Intradermal Injections - cont.):

c. Administration:

Substances were administered by intradermal injection, using a 1.0 cc syringe and a 25 or 26 gauge 5/8" needle, in the clipped shoulder area. One row of three injections was made on each side of the spinal column, for a total of six injections. Injections 1 and 2 were given close together and nearest to the head; injection 3 was given most caudally. 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 in propylene glycol or propylene glycol alone, per site.
- (3) Two sites with 0.1 mL of test material in FCA/water emulsion or propylene glycol in FCA/water, per site.

The injections were made within the boundaries of the 2x4 cm area over which a patch was applied the following week. (Note: Irritation control animals received FCA/water emulsion and/or vehicle only.)

2. Day 8 (Topical Application):

a. Preparation of Animals:

The hair in the shoulder area was re-clipped on the day of topical application. The area was pretreated with 10% sodium lauryl sulfate (SLS) in petrolatum [0.1 g/g (10% w/w)] on the day before the test patch was applied in order to provoke a mild inflammatory reaction. (The SLS was massaged into the skin with gloved fingers).

b. Preparation of Test Material:

Group 1: The test material was administered as received; no preparation was necessary.

Group 2: Propylene glycol was administered as received; no preparation was necessary.

VI. METHODS (cont.)

F. Administration of Test and Control Materials (cont.):

2. Day 8 (cont.):

c. Administration:

The test or control material or vehicle was applied to a 2x4 cm filter paper to saturation (approximately 0.2 mL). The filter paper was then placed on the test site and covered by overlapping impermeable plastic, which was firmly secured by an elastic adhesive bandage 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 with 0.9% saline and gauze.

3. Day 22 (Challenge):

a. Preparation of Animals:

The hair was removed from a 5x5 cm area on the flank, by clipping as described previously, on the day of the Challenge application.

b. Preparation of Test Material:

Groups 1 and 2:

Site 5: The test material was administered as received; no preparation was necessary.

Site 6: The appropriate amount of propylene glycol was added to MCP 1286 to produce a 0.5 mL/mL (50% v/v) mixture.

c. Administration:

(1) Test Animals:

Patches were applied to the flank using the same procedures as for topical application on Day 8, except that a 2x2 cm piece of filter paper was used (saturated with approximately 0.1 mL of test material) and allowed to remain on the animal for 24 hours. Two concentrations were applied for a total of two sites per animal. Dose sites were wiped free of excess test material with 0.9% saline and gauze. Dermal readings were made on all

VI. METHODS (cont.)

F. Administration of Test and Control Materials (cont.):

3. Day 22 (cont.):

c. Administration (cont.):

(1) Test Animals (cont.):

animals 24 and 48 hours after the removal of the patches (the area was gently clipped after the 24 hour evaluation).

(2) Irritation Control Animals:

In order to differentiate dermal reactions produced by irritation from those produced by sensitization, 5 males previously treated with the FCA/water emulsion and vehicle only, were subjected to the same Challenge procedures as the animals which received the induction exposures to the test material.

VII. EXPERIMENTAL EVALUATION

A. Viability Check (in-cage):

Observations for mortality were made twice daily.

B. Body Weights:

Pretest (day of first Induction)
Termination (three days after Challenge)

C. Observations:

Animals were observed prior to treatment and weekly during the study for general health; unusual observations were recorded.

D. Evaluation of Dermal Responses:

1. Intervals:

Dermal evaluations were made approximately 24 hours after each Induction (intra-dermal and topical - after removal of patches) and 24 and 48 hours after removal of Challenge patches.

VII. EXPERIMENTAL EVALUATION (cont.)

D. Evaluation of Dermal Responses (cont.):

2. Methods:

Reactions were scored according to the scoring system presented in Appendix B.

VIII. POSTMORTEM

All animals were sacrificed by carbon dioxide inhalation and discarded. No postmortem examinations were performed.

IX. EVALUATION OF RESULTS

Redness at the Challenge site which is clearly 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.

In order to evaluate the responses, two indices were used, one for incidence and one for severity, for both test and control animals. The Incidence Index is an expression of the number of animals showing a response grade of one or greater at either 24 or 48 hours out of the total number of animals in the group and is the basis for classifying the allergenicity potency of the test material, as defined in the publication on which this test is based (Magnusson and Kligman, op. cit.).

Allergenicity Rating		
Incidence Index (%)	Grade	Classification
1 - 8	I	Weak
9 - 28	II	Mild
29 - 64	III	Moderate
65 - 80	IV	Strong
81 - 100	V	Extreme

IX. EVALUATION OF RESULTS (cont.)

The Severity Index is determined for both the 24- and 48-hour response readings by dividing the sum total of grades in a given group by the number of animals exposed.

The test material is considered a "risk phrase R43", under EEC criteria (Commission directive 93/12/EEC), if there is a positive response in at least 30% of the animals.

X. STATISTICAL ANALYSIS

No statistical analysis of the data was performed.

XI. PROTOCOL DEVIATIONS

There were no protocol deviations.

XII. RESULTS AND DISCUSSION

A. Mortality

All animals survived throughout the study.

B. Body Weights (Table I)

All animals gained weight throughout the study.

C. Dermal Responses (Tables II, III and IV)

1. Induction (Table II)

Responses seen during the Induction phase were typical responses seen in this study design and are probably due to administration of FCA.

2. Challenge (Tables III and IV)

Five of the ten animals challenged with neat test material exhibited clear dermal responses (scores of 1 or greater) and the remaining five animals exhibited scores of less than 1. Four of the test animals also exhibited edema. One irritation control animal exhibited a clear dermal response (score of 1) and the remaining four irritation control animals were free of dermal responses. The Incidence Index of Sensitization to the test material at Challenge was 50%. The Severity Indices for the test group at 24 and 48 hours were both 0.5. For the irritation control groups at 24 and 48 hours, the Indices were 0.0 and 0.2, respectively.

Seven of ten animals challenged with a 50% concentration of exhibited clear dermal responses (scores of 1 or greater) and the remaining three animals exhibited scores of less than 1. All five irritation control animals were free of significant dermal responses. The Incidence Index of Sensitization to a 50% concentration of the test

XI. RESULTS AND DISCUSSION (cont.)

C. Dermal Responses (cont.)

2. Challenge (cont.)

material at Challenge was 70%. The Severity Indices for the test group at 24 and 48 hours were 0.7 and 0.9, respectively, and for the irritation control groups at 24 and 48 hours were 0.1 and 0.2, respectively.

XIII. CONCLUSION

Under conditions of this study, _____ exhibited a potential to produce dermal sensitization in guinea pigs and would be considered a "risk phrase R43" according to the EEC criteria.



Diann L. Blanset, M.S., D.A.B.T.
Study Director/Toxicologist

20 Jan 98

Date



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

20 Jan 98

Date

Table I
: Guinea Pig Maximization Test

Body Weights (grams)

<u>Group</u>	<u>Animal No. and Sex</u>	<u>Pretest</u>	<u>Terminal</u>	<u>Weight Gain</u>
1 Test Animals	4539 M	396	535	139
	4540 M	419	577	158
	4541 M	406	528	122
	4542 M	424	538	114
	4543 M	423	514	91
	4544 M	451	610	159
	4545 M	446	586	140
	4546 M	427	575	148
	4547 M	420	551	131
4548 M	420	486	66	
2 Irritation Control Animals	4549 M	407	548	141
	4550 M	418	515	97
	4551 M	476	645	169
	4552 M	485	647	162
	4553 M	458	593	135

M=Male.

Table II
: Guinea Pig Maximization Test

Individual Dermal Scores at Inductions ^a			
<u>Group</u>	<u>Animal No. and Sex</u>	<u>Intradermal^b 24 Hrs</u>	<u>Topical 24 Hrs</u>
1 Test Animals	4539 M	3 B, Ed	3 B, Ed
	4540 M	3 B, Ed	3 B, Ed
	4541 M	3 B, Ed	3 B, Ed
	4542 M	3 B, Ed	3 B, Ed
	4543 M	3 B, Ed	3 B, Ed
	4544 M	3 B, Ed	3 B, Ed
	4545 M	3 B, Ed	3 B, Ed
	4546 M	3 B, Ed	3 B, Ed
	4547 M	3 B, Ed	3 B, Ed
	4548 M	3 B, Ed	3 B, Ed
2 Irritation Control Animals ^c	4549 M	3 B, Ed	3 B, Ed
	4550 M	3 B, Ed	3 B, Ed
	4551 M	3 B, Ed	3 B, Ed
	4552 M	3 B, Ed	3 B, Ed
	4553 M	3 B, Ed	3 B, Ed

^aScored using the scoring system presented in Appendix B.

^bFor the intradermal induction, an overall score for all three injection sites was assigned. Refer to experimental design for details regarding each site.

^cIrritation control animals were not treated with the test material during the Induction phase.

M=Male; B=Black/Dark Tissue; Ed=Edema.

Table III
Guinea Pig Maximization Test

Incidence of Dermal Responses at Challenge															
Group	Material	Conc. ^b	Hrs.	Dermal Scores ^a									P ^c	IIS ^d	Tot.# of Animals
				0	0.5	1	2	3	Ed	E	W	B			
1		100%	24	2	6	2	0	0	3	0	0	0	5	50	10
			48	4	3	3	0	0	3	0	0	0			
2	(Irritation Control) ^e	100%	24	5	0	0	0	0	0	0	0	0	1		5
			48	4	0	1	0	0	1	0	0	0			
1		50%	24	1	4	5	0	0	6	0	0	0	7	70	10
			48	1	5	2	2	0	7	0	0				
2	(Irritation Control) ^e	50%	24	4	1	0	0	0	0	0	0	0			5
			48	3	2	0	0	0	0	0	0	0			

^aScored using the scoring system presented in Appendix B.

^bConc.-Concentration administered at challenge.

^cP-Positive response; number of animals with a score of 1 or greater at 24 and/or 48 hours, out of the 10 animals per group.

^dIncidence Index of Sensitization=P/N x 100, where N=total number of animals.

^eIrritation control groups were treated with test material at challenge only.

Table IV
Guinea Pig Maximization Test

Individual Dermal Scores at Challenge ^a Groups 1 and 2 Material: MCP 1286 Challenge Concentration: 100%					
Group 1			Group 2		
Animals Treated During Induction			Irritation Control Animals ^b		
Animal No. and Sex	Interval		Animal No. and Sex	Interval	
	24 Hours	48 Hours		24 Hours	48 Hours
4539 M	0.5	1	4549 M	0	0
4540 M	0.5	1	4550 M	0	0
4541 M	1 Ed	0	4551 M	0	0
4542 M	0	0	4552 M	0	0
4543 M	0	0	4553 M	0	1 Ed
4544 M	0.5	0.5			
4545 M	0.5 Ed	1 Ed			
4546 M	0.5	0			
4547 M	1	0.5 Ed			
4548 M	0.5 Ed	0.5 Ed			
Sum of Scores:	5.0	4.5		0.0	1.0
Mean ^c :	0.5	0.5		0.0	0.2

^aScored using the scoring system presented in Appendix B.

^bIrritation control animals were treated with test material at challenge only.

^cMean=Severity Index.

M=Male; Ed=Edema.

Table IV (cont.)

Guinea Pig Maximization Test

Individual Dermal Scores at Challenge ^a					
Groups 1 and 2					
Material: MCP 1286					
Challenge Concentration: 50%					
Group 1			Group 2		
Animals Treated During Induction			Irritation Control Animals ^b		
Animal No. and Sex	Interval		Animal No. and Sex	Interval	
	24 Hours	48 Hours		24 Hours	48 Hours
4539 M	0.5 Ed	2 Ed	4549 M	0	0
4540 M	0.5	1 Ed	4550 M	0.5	0.5
4541 M	1 Ed	0.5 Ed	4551 M	0	0
4542 M	0.5 Ed	0.5	4552 M	0	0.5
4543 M	0	0	4553 M	0	0
4544 M	1	2 Ed			
4545 M	1 Ed	0.5 Ed			
4546 M	1	0.5			
4547 M	1 Ed	1 Ed			
4548 M	0.5 Ed	0.5 Ed			
Sum of Scores:	7.0	8.5		0.5	1.0
Mean ^c :	0.7	0.9		0.1	0.2

^aScored using the scoring system presented in Appendix B.

^bIrritation control animals were treated with test material at challenge only.

^cMean=Severity Index.

M=Male; Ed=Edema.

Appendix A
Guinea Pig Maximization Test

Range-Finding Studies

Intradermal Injections ^a				
Animal No. and Sex	Site #1 (5.0%) ^b		Site #2 (5.0%) ^b	
	24 Hours	48 Hours	24 Hours	48 Hours
4537 M	3 B, Ed	3 B, Ed	3 B, Ed	3 B, Ed
4538 M	3 B, Ed	3 B, Ed	3 B, Ed	3 B, Ed

Topical Application ^a								
Animal No. and Sex	Concentration							
	100%		75% ^b		50% ^b		25% ^b	
	24 Hours	48 Hours	24 Hours	48 Hours	24 Hours	48 Hours	24 Hours	48 Hours
4455 M	0.5	0.5	0.5	0.5	0	0	0.5	0
4456 M	0	0	0	0	0	0	0	0
4477 M	0	0	0	0	0	0	0	0
4478 M	0.5	0	0	0	0	0	0	0

^aScored using the scoring system presented in Appendix B.

^bVehicle: propylene glycol.

M=Male; B=Black/Dark Tissue; Ed=Edema.

Appendix B

Guinea Pig Maximization Test

Evaluation of Dermal Responses

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

If edema, tissue damage or eschar formation occurred, they were also indicated using the following code:

Edema.....	Ed
White Tissue.....	W
Black/dark Tissue....	B
Eschar.....	E

Appendix C

Guinea Pig Maximization Test

Historical Control Data - Study No. 4
 Sensitization of Guinea Pigs to Hexylcinnamic Aldehyde (HCA)
 (Method of Magnusson and Kligman)
 7 October 1997 - 1 November 1997
 Individual Dermal Scores at Challenge^a
 Challenge Concentration: 100%

<u>Animals Treated During Induction</u>			<u>Irritation Control Animals^b</u>		
<u>Animal No. and Sex</u>	<u>Interval</u>		<u>Animal No. and Sex</u>	<u>Interval</u>	
	<u>24 Hours</u>	<u>48 Hours</u>		<u>24 Hours</u>	<u>48 Hours</u>
4556 M	1	0.5	4561 M	0.5	0
4557 M	1	0	4562 M	0.5	0
4558 M	1 Ed	1	4563 M	0	0
4559 M	0.5	0	4564 M	0	0
4560 M	1	0	4565 M	0	0
4593 F	1 Ed	0.5	4598 F	0	0
4594 F	2 Ed	1 Ed	4599 F	0	0
4595 F	0.5	0	4600 F	0	0
4596 F	1 Ed	0	4601 F	0.5	0
4597 F	0.5	1 Ed	4602 F	0	0
Sum of Scores:	9.5	4.0		1.5	0.0
Mean ^c :	1.0	0.4		0.2	0.0
Number Sensitized ^d :	8/10				
Percent Sensitized ^e :	80%				

^aScored using the scoring system presented in Appendix B.

^bIrritation control animals were treated with control material at Challenge only.

^cMean=Severity Index.

^dAnimals were considered sensitized if they exhibited a dermal score of 1 or greater.

^ePercent Sensitized=Incidence Index of Sensitization.

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

Appendix D
Guinea Pig Maximization Test

Quality Assurance Statement

Listed below are dates that this study was inspected by the Quality Assurance Unit of Huntingdon Life Sciences, East Millstone, New Jersey, and the dates that findings were reported to the Study Director and Management.

<u>Type of Inspection</u>	<u>Date(s) of Inspection</u>	<u>Reported to Study Director and Management</u>
Dose Administration and Pharmacy File	70ct97	90ct97
Report	15Dec97 and 16Dec97	16Dec97



Terrence T.A. Gittens, B.A., AALAS LAT
Quality Assurance Auditor

12 Jan 98

Date

Appendix E

: Guinea Pig Maximization Test

Statement of Compliance

This study does not meet all the requirements of the Organization for Economic Cooperation and Development [OECD - (Annex 2 C(81)30 Final)] or European Economic Community [EC Council Directive, 87/18 EEC of 18 Dec 86, (No. L 15/29)] and differs in the following way:

Assay to verify concentration, stability and homogeneity of the test material in the carrier was not performed.



Diann L. Blanset, M.S., D.A.B.T.
Study Director/Toxicologist

20 Jan 98

Date

Appendix F
Guinea Pig Maximization Test

Report Amendments

There are no amendments for this report at this time.