

METHACRYLATE PRODUCERS ASSOCIATION, INC.

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February 24, 1997

via messenger

PDCN: 88960000229

8EHQ-0297-13749

Document Control Office (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Room G-099
401 M Street, SW
Washington, DC 20460



8EHQ-96-13749

97 FEB 24 PM 2:03

RECEIVED
OPPT NCIC

Re: Notice in Accordance with TSCA Section 8(e) - Results of DOT Skin Irritation Test with Methacrylic Acid (MAA) in New Zealand Rabbits: (CAS No. 79-41-4)

97 FEB 28 AM 8:37

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OPPT NCIC

Dear Sir/Madam:

On September 25, 1996, the Methacrylate Producers Association (MPA) submitted preliminary results from a DOT skin irritation test with methacrylic acid (CAS No. 79-41-4) in accordance with TSCA Section 8(e). Enclosed are six copies of the final report for the study entitled "Methacrylic Acid: Skin Irritation Study in Rabbits."

This submission is being made on behalf of the MPA member companies: CYRO Industries, Elf Atochem N.A., Inc., ICI Acrylics, Inc., and Rohm and Haas Company. If you have any questions about this submission, please contact me at (202) 962-9486.

Contains No CBi

Sincerely,

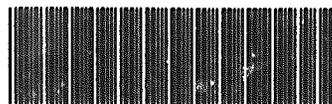
Elizabeth K. Hunt

Elizabeth K. Hunt
Executive Director

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cc: MPA



89970000088

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 **Report No. 96R-132**

J.R. Parno

Report Final: December 19, 1996

Applicable Guidelines:
OECD Guideline 404
US EPA 40 CFR Section 798.4470
EEC Directive 92/69/EEC B.4
U.S. D.O.T. Section 173.137

Rohm and Haas Company
Toxicology Department
727 Norristown Road
P. O. Box 904
Spring House, PA 19477-0904

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Skin Irritation Study in Rabbits
Protocol No. 96P-132 **Report No. 96R-132**

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REGULATORY/COUNTRY REQUIREMENTS**

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Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132**

QUALITY ASSURANCE STATEMENT

This final report and the original raw data were reviewed for adherence to Good Laboratory Practices. This report is an accurate reflection of the raw data and an accurate description of the methods and standard operating procedures from this study. The following inspections were performed and reported to the Study Director and management:

<u>Inspections Performed</u>	<u>Dates</u>	
	<u>Inspected</u>	<u>Reported</u>
Dosing	July 23, 1996	September 18, 1996
Draft Report	November 25, 1996	November 25, 1996
Final Report	Dec. 19, 1996	Dec. 19, 1996
	<u>B.A. Decker, p.c.</u>	<u>Dec. 19, 1996</u>
	B.A. Decker, B.S., Analyst	Date
	Quality Assurance Unit	
	Rohm and Haas Company	

GLP COMPLIANCE STATEMENT

The study described in this final report was conducted in compliance with the following Good Laboratory Practice Standards except that chemical characterization of the test substance under a GLP Program was not conducted prior to the initiation of the study:

United States Environmental Protection Agency, Title 40 CFR Part 792, Toxic Substances Control act, published in the Federal Register, August 17, 1989;

Japan Ministry of Agriculture, Forests and Fisheries, 59 NohSan Notification No. 3850, Agricultural Production Bureau, August 10, 1984;

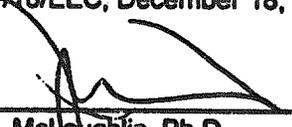
Organization for Economic Cooperation and Development, ISBN 92-64-12367-9, Paris 1992;

European Economic Community, Council Directive 87/18/EEC, December 18, 1986.



J.F. Parno, M.S.
Study Director
Rohm and Haas Company

19. DEC. 96
Date



J.E. McLaughlin, Ph.D.
Sponsor
Rohm and Haas Company

12/19/96
Date



H.E. Scribner, Ph.D., D.A.B.T.
Director of Toxicology
Rohm and Haas Company

12/19/96
Date

Methacrylic Acid
Skin Irritation Study in Rabbits
Protocol No. 96P-132 Report No. 96R-132



J.R. Parno, M.S.
Study Director
Rohm and Haas Company

19-DE-76
Date

Report Final: December 19, 1996

Rohm and Haas Company
Toxicology Department
727 Norristown Road
P. O. Box 904
Spring House, PA 19477-0904

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KEY PERSONNEL PARTICIPATING IN THE STUDY

<u>Name</u>	<u>Responsibility</u>
J.R. Parno	Study Director
M.F. Lutz	Principal Investigator
L.P. Craig	Study Coordinator
K.B. Poorman	Animal Care Supervisor

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ABSTRACT

Skin irritation of methacrylic acid (Lot No. 6/4/96, Toxicology Department Sample No. 96-054, 99.38% active ingredient) was assessed in New Zealand White rabbits. The undiluted test substance (0.5 ml) was applied topically to the shaved intact skin of one male rabbit. The application site was semi-occluded for 4 hrs. After the 4 hr exposure, the application site was wiped with paper towels saturated with tap water and blotted dry with paper towels. Skin irritation was evaluated according to Draize criteria at approximately 1, 24, 48, 72 hrs and at 7 and 14 days after patch removal. No mortality or clinical signs of systemic toxicity were observed during the study. Severe erythema and skin effects indicative of corrosivity (i.e., concave eschar) were observed. According to the Rohm and Haas Company Acute Toxicity and Irritation Hazard Categories (September, 1994), methacrylic acid is categorized as CORROSIVE to skin (i.e., evidence of irreversible destruction of dermal tissue).

Since corrosive findings were evident at 4 hrs, additional rabbits were tested to determine U.S. Department of Transportation (DOT) Packing Group classification. The undiluted test substance (0.5 ml) was applied topically to the shaved intact skin of one male rabbit on two separate sites for 1 hr (left side) and 3 minutes (right side). The 1 hr application site was semi-occluded with a fabric cuff and the 3 minute site was uncuffed during the exposure period. After each exposure period, the application sites were wiped with paper towels saturated with tap water and blotted dry with paper towels. Two additional rabbits received either a 1 hr or 3 minute exposure. A 1% soap solution was used on the additional rabbits exposed for the 1 hr or 3 minute period prior to the tap water rinse to assess whether more complete washing would prevent corrosivity. Skin irritation was evaluated according to Draize criteria at approximately 1, 24, 48, 72 hrs and at 7 and/or 14 days after patch removal. Severe erythema and skin effects indicative of corrosivity (i.e., concave eschar and erosion/ulceration) were observed on the 1 hr and 3 minute sites. According to D.O.T. Packing Group Classification guidelines for Class 8 materials (June, 1990), methacrylic acid is assigned to PACKING GROUP I (i.e., corrosive at the site of contact when tested on the intact skin of rabbits for a period of not more than 3 minutes).

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I. INTRODUCTION

This study was conducted to determine the skin irritation of methacrylic acid when applied to the shaved intact skin of rabbits. The study initiation (date protocol signed by Study Director) was July 18, 1996. The experimental start (day of dosing) and experimental termination (last day of observation) dates were July 23, 1996 and October 8, 1996, respectively.

II. MATERIALS AND METHODS

A. Experimental Design

<u>Test Substance</u>	<u>Exposure</u>	<u>Dose</u>	<u>No. of Rabbits</u>
methacrylic acid	4 hrs	0.5 ml	1
methacrylic acid	1 hr	0.5 ml	2
methacrylic acid	3 min.	0.5 ml	2

The test substance was applied as received and the application sites were semi-occluded for the 4 and 1 hour exposure. The 3 minute site was left uncuffed during the exposure period.

B. Test Substance

The test substance, identified as methacrylic acid (Lot No. 6/4/96, assigned Rohm and Haas Toxicology Department Sample No. 96-054), was a clear liquid containing 99.38% active ingredient.

C. Animals and Animal Husbandry

Adult male New Zealand White rabbits were obtained from Hazleton Research Animals, Denver, PA. Upon arrival, all animals were examined for physical abnormalities, identified by uniquely numbered ear tags, and quarantined for approximately two weeks. The animals were individually housed in stainless steel cages (18x24x14.5 in., i.e. 46x61x37 cm) suspended above absorbent-paper pan liners which were changed 3 times per week. Throughout the test period, all rabbits had free access to filtered tap water (via automatic watering) and were fed

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C. Animals and Animal Husbandry (Cont'd)

approximately 125 g/day of PMI Certified High Fiber Rabbit Diet 5325 (Purina Mills Inc., Richmond, IN). All animal rooms were environmentally controlled with controls set to maintain a temperature of approximately 65°F (18°C) and a relative humidity range of 30-70%. The temperature and relative humidity were monitored 24 hrs a day. During the study, the average daily temperature ranged from 64 to 66°F (18 to 19°C) and average daily humidity ranged from 54 to 68%. Excursions beyond these ranges were minimal and did not affect the integrity of the study. Temperature and humidity remained in compliance with acceptable ranges defined in the "Guide for the Care and Use of Laboratory Animals" NIH Publication No. 86-23, Revised 1996. The light cycle was automatically controlled, 12 hrs on and 12 hrs off.

One day prior to dosing, rabbits were selected from a healthy stock population. At the time they were dosed, the animals were approximately 19 to 30 weeks old and their body weights ranged from 2733 to 3484 g.

D. Dose Preparation and Administration

Approximately 24 hrs prior to the application of the test substance, the hair around the entire trunk between the flank and shoulders was shaved closely with electric clippers. The undiluted test substance (0.5 ml) was applied onto a 1.0-in. square gauze-lined adhesive bandage which was applied to the shaved intact skin of one rabbit for 4 hrs. A semi-occluded dressing (i.e., fabric cuff secured with adhesive tape) was used to wrap the entire trunk of the animal. The rabbit was returned to its cage for a 4 hr exposure period. An additional rabbit was tested on two separate sites for a 1 hr (right side) and 3 minute (left side) exposure. The 1 hr site was treated in the same manner as the 4 hr. The animal remained uncuffed during the 3 minute exposure. The cuff and patch were removed after the appropriate exposure and the application site wiped with paper towels saturated with tap water. The application site was blotted dry with paper towels. Two additional rabbits were tested for either a 1 hr or 3 minute exposure in the same manner as described above except these rabbits were washed with a 1% Ivory® soap solution prior to the tap water rinse.

E. Observations and Determinations

Skin irritation was evaluated at approximately 1, 24, 48, 72 hrs and at 7 and/or 14 days after patch removal. The degree of irritation was evaluated according to the

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E. Observations and Determinations (Cont'd)

criteria of Draize *et al.* (*J. Pharmacol. Exp. Therap.* **82**, 377-390, 1944), which are summarized in Appendix A. DOT Packing Group Classification guidelines are shown in Appendix B. In addition, all other skin reactions or signs of systemic toxicity were recorded. Animals were observed daily for mortality and reaction to treatment.

F. Location of Raw Data

All raw data, supporting documents, and records are stored in the Archives of the Toxicology Department, Rohm and Haas Company, 727 Norristown Road, P. O. Box 904, Spring House, PA 19477-0904.

III. RESULTS

Individual skin irritation scores (Draize criteria) are presented in Tables 1, 2 and 3. No mortality or clinical signs of systemic toxicity (other than skin effects) were observed during the study.

On all sites (4 hr, 1 hr and 3 minute), skin irritation indicative of corrosivity (i.e., concave eschar) was observed. On the 4 hr exposure site, severe erythema and very slight to severe edema was evident at all observation periods (1 of 1 rabbit). On the 1 hr site, severe erythema and very slight to moderate edema was observed at all observation periods (2 of 2 rabbits). One of these rabbits was euthanized after 24 hr scores due to the severity of the damage to the dermis (the subcutaneous muscle layer was visible and reddened). On the 3 minute site, severe erythema and very slight to moderate edema was evident at all observation periods (2 of 2 rabbits). One of these rabbits was euthanized after day 7 scores when conclusive evidence of irreversible damage (i.e. concave eschar, erosion and ulceration) was noted.

Washing the sites (1 hr or 3 minute) with a 1% soap solution did not affect the outcome of the study (corrosive effects were evident in animals receiving either the tap water rinse or the soap and water rinse).

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IV. CONCLUSIONS

According to the Rohm and Haas Company Acute Toxicity and Irritation Hazard Categories (September, 1994), methacrylic acid is categorized as **CORROSIVE** to skin following a 4 hr exposure period (i.e., evidence of irreversible destruction of dermal tissue).

According to DOT Packing Group Classification guidelines for Class 8 materials (June, 1990), methacrylic acid is assigned to **PACKING GROUP I** (i.e., corrosive at the site of contact when tested on the intact skin of rabbits for a period of not more than 3 minutes).

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Table 1. Skin Irritation Scores (Draize Criteria)† - 4 Hr

ERYTHEMA:		Time After Patch Removal											
<u>Animal No.</u>		<u>1 hr</u>		<u>24 hrs</u>		<u>48 hrs</u>		<u>72 hrs</u>		<u>7 days</u>		<u>14 days</u>	
96-27222		4	ab	4	abc	4	abc	4	abc	4	abcd	4	acd
EDEMA:													
<u>Animal No.</u>													
96-27222		4		3		2		1		1		1	

† Scoring criteria is presented in Appendix A.

- a. Blackened
- b. Test substance adhered
- c. Application site perimeter: reddened
- d. Concave eschar

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Table 2. Skin Irritation Scores (Draize Criteria)† - i Hr

ERYTHEMA:	Time After Patch Removal						
	Animal No.	1 hr	24 hrs	48 hrs	72 hrs	7 days	14 days
	96-27199	4 ef	4 ef	4 ef	4 ef	4 def	4 def
	96-27242	4 a	4 g	-	-	-	-
EDEMA:							
	Animal No.						
	96-27199	3	3	2	2	1	1
	96-27242	3	3	-	-	-	-

† Scoring criteria is presented in Appendix A.

a. Skin pulled off at time of patch removal

d. Concave eschar

e. Application site perimeter: reddened

f. Application site perimeter: blanching

g. All layers of dermis destroyed. Subcutaneous muscle layer visible and reddened.

(-) No applicable data. Animal was euthanized after 24 hr scores due to the severity of the damage to the dermis.

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Table 3. Skin Irritation Scores (Draize Criteria)† - 3 Minute

ERYTHEMA:		Time After Patch Removal					
Animal No.	1 hr	24 hrs	48 hrs	72 hrs	7 days	14 days	
96-27199	4 e	4 ef	4 ef	4 ef	4 def	4 def	
96-27243	4 f	4 cf	4 cd	4 cd	4 cd	-	
EDEMA:							
Animal No.	1 hr	24 hrs	48 hrs	72 hrs	7 days	14 days	
96-27199	3	3	2	2	1	1	
96-27243	3	3	2	1	1	-	

† Scoring criteria is presented in Appendix A.

c. Blackened

d. Concave eschar

e. Application site perimeter: reddened

f. Application site perimeter: blanching

(-) No applicable data. Animal was euthanized after Day 7 scores when conclusive evidence of irreversible damage to the dermis was noted.

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Appendix A. Skin Irritation Scoring (Draize Criteria)

Erythema Scores (Maximum = 4)

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 Scores (Maximum = 4)

No edema.....	0
Very slight edema (barely perceptible)	1
Slight edema (edges of area well-defined by definite raising).....	2
Moderate edema (area raised approximately 1 mm).....	3
Severe edema (raised more than 1 mm and extending beyond area of exposure).....	4

Skin irritation is categorized on the basis of the Primary Irritation Index (PII). The PII is the sum of the erythema and edema scores at 1, 24, 48 and 72 hr divided by the number of observations (4), then divided by the number of animals (6).

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Appendix B. United States Department of Transportation Packing Group Classification Criteria¹

Packing Group	Classification Criteria
I	Corrosivity* in not more than 3 minutes in at least 2 of 6** rabbits tested.
II	Corrosivity in greater than 3 minutes but not more than 1 hour in at least 2 of 6 rabbits tested.
III	Corrosivity in greater than 1 hour but not more than 4 hours in at least 2 of 6 rabbits tested.

*Corrosivity: Destruction or irreversible alterations of the skin tissue at the site of contact when tested on the skin of an animal.

**Only 2 rabbits were tested since corrosive effects were evident in the first 2 rabbits exposed for 1 hr and 3 minutes.

¹D.O.T. (1990) U.S. Department of Transportation, *Method of Testing Corrosion to Skin*, Federal Register, Section 173.137 (June 1990).