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RHÔNE-POULENC INC.

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September 4, 1992

**CERTIFIED MAIL
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Document Processing Center (TS-790)
Attn: Section 8(e) Coordinator (CAP Agreement)
Office of Toxic Substances
Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

CAP ID NO.: 8ECAP - 0004

RP CAP REPORT NO.: RPS - 0200

Dear Sir/Madam:

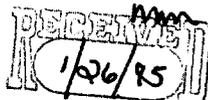
On behalf of Rhône-Poulenc Inc. (RPI, CN5266, Princeton, NJ 08543-5266) and its subsidiaries, the attached report is being submitted to the Environmental Protection Agency (EPA) pursuant to the Toxic Substances Control Act (TSCA) Section 8(e) Compliance Audit Program (CAP Agreement) executed by RPI and EPA (8ECAP - 0004).

The enclosed report provides information on the following chemical substance:

Chemical Identity: Hydroxyethyl acrylate (HEA)
(Coded as SN-1509 in the report)

CAS Registry No: 818-61-1

CAS Registry Name: 2-Propenoic acid, 2-hydroxyethyl ester



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The title of the enclosed report is:

Acute Toxicity Studies With SN-1509

The following is a summary of the adverse effects observed in this report.

The test material was extremely irritating to the unwashed eyes of albino rabbits in the eye irritation study. The reactions increased in severity through Day 14. In the primary skin irritation test with albino rabbits, the test material was extremely irritating, causing third degree chemical burns and subdermal hemorrhage in all animals.

The acute dermal LD50 was 298 mg/kg and was classified as moderately toxic. Second and third degree chemical burns and subdermal hemorrhages were noted at Day 7, and at Day 14, necrosis was observed. Clinical signs observed in the dermal toxicity study included hypoactivity, muscular weakness, loss of righting reflex, hypothermia, and mydriasis.

RPI does not claim any portion of the information in this submission to be TSCA confidential business information (TSCA CBI).

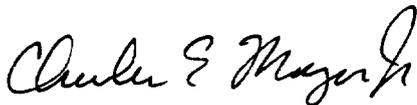
RPI has not previously submitted any TSCA Section 8(e) notices or premanufacture notification on the subject chemical substance.

RPI has submitted another study on this material under the CAP agreement; see RP CAP Report No. RPS-0199.

On August 15, 1985, Celanese submitted to EPA all available toxicity data on the multifunctional acrylates. However, RPI does not have a detailed list in our records of the reports that were submitted. Therefore, RPI is submitting three copies of the enclosed report and this cover letter: an original and two copies.

Further questions regarding this submission may be directed to Dr. Glenn S. Simon, Director of Toxicology at (919)549-2222 (Rhône-Poulenc, P.O. Box 12014, 2 T.W. Alexander Drive, Research Triangle Park, NC 27709).

Sincerely,



Charles E. Moyer, Jr., Ph.D.
Director, Product Safety
(609)860-3589

CAP ID No. S-LT-PW-0028
Reviewed for Sec. 8 (e)
Compliance Program
On 10/4/91 By PN

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REPORT TO
CELANESE CORPORATION
ACUTE TOXICITY STUDIES WITH
SN-1509

MAY 9, 1974

IBT NO. 601-04930

I. Introduction

A sample identified as Hydroxyethyl Acrylate, SN-1509 was received from Celanese Corporation for toxicological evaluation. The following studies were conducted:

- Acute Oral Toxicity Study - Albino Rats
- Acute Dermal Toxicity Study - Albino Rabbits
- Eye Irritation Test - Albino Rabbits
- Primary Skin Irritation Test - Albino Rabbits

II. Summary

The results of the acute toxicity studies with Hydroxyethyl Acrylate, SN-1509 are summarized below.

<u>Test</u>	<u>Results</u>
Acute Oral Toxicity Study - Albino Rats	Slightly Toxic LD ₅₀ = 548.0 mg/kg 95% Confidence Limits of LD ₅₀ = 460.5 - 652.1 mg/kg
Acute Dermal Toxicity Study - Albino Rabbits	Moderately Toxic LD ₅₀ = 298.0 mg/kg 95% Confidence Limits of LD ₅₀ = 220.7 - 402.3 mg/kg
Eye Irritation Test - Albino Rabbits	Extremely Irritating (96.7/110)
Primary Skin Irritation Test - Albino Rabbits	Extremely Irritating (8.0/8.0)

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by: Carol Hintz
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III. Investigational Procedures

The detailed investigational procedures employed in these studies are presented in the appendix.

IV. Results

A. Acute Oral Toxicity Study - Albino Rats

1. Mortality and Body Weights

Individual mortality and body weight data are presented in Table I.

TABLE I

Acute Oral Toxicity Study - Albino Rats

Mortality and Body Weight Data

Test Material: SN-1509

Form Administered: 10.0% (w/v) aqueous solution

Acute Oral LD₅₀ = 548.0 mg/kg, expressed in terms
of SN-1509

Strain: Sprague-Dawley

IBT No.: 601-04930

Classification: Slightly
Toxic95% Confidence Limits of LD₅₀ = 460.5 - 652.1 mg/kg

Dose Level (mg/kg)	Animal Number and Sex	Individual Body Weights (grams)		Number Dead / Number Tested	Percent Dead
		Test Day Number:			
		0	14		
266.7	1-M	163	278	0/4	0
	2-M	162	274		
	3-F	152	192		
	4-F	161	205		
400.0	5-M	162	252	0/4	0
	6-M	154	238		
	7-F	159	189		
	8-F	160	194		
600.0	9-M	168	(6-22 hours)	3/4	75
	10-M	157	(6-22 hours)		
	11-F	167	208		
	12-F	151	(6-22 hours)		
900.0	13-M	168	(6-22 hours)	4/4	100
	14-M	167	(6-22 hours)		
	15-F	161	(6-22 hours)		
	16-F	155	(6-22 hours)		

Note: Figures in parentheses indicate time of death.

2. Reactions

The untoward reactions exhibited by the rats following dosing are presented in Table II.

Necropsy examination of the animals that died revealed hemorrhages in the gastrointestinal tracts. No gross pathologic alterations were noted among the animals sacrificed at the end of the 14-day observation period.

TABLE II

Acute Oral Toxicity Study - Albino Rats

Summary of Reactions

Test Material: SN-1509
 Concentration: 10.0% (w/v) aqueous solution

IBT No.: 601-04930

Dose Level (mg/kg)	Reaction	Time of Onset Following Dose Administration	Duration of Reaction	Time of Death Following Dose Administration
266.7	Hypoactivity	30 minutes	6-22 hours	-
	Ruffed fur	30 minutes	6-22 hours	-
400.0	Hypoactivity	30 minutes	2 days	-
	Ruffed fur	30 minutes	2 days	-
	Labored breathing	1 hour	6-22 hours	-
600.0	Hypoactivity	30 minutes	4 days	6-22 hours
	Ruffed fur	30 minutes	4 days	
	Labored breathing	1 hour	2 days	
	Muscular weakness	1 hour	2 days	
900.0	Hypoactivity	30 minutes	Until death	6-22 hours
	Ruffed fur	30 minutes		
	Labored breathing	1 hour		
	Muscular weakness	1 hour		

B. Acute Dermal Toxicity Study - Albino Rabbits

1. Mortality and Body Weights

Individual mortality and body weight data are presented in Table III.

TABLE III

Acute Dermal Toxicity Study - Albino Rabbits

Mortality and Body Weight Data

Test Material: SN-1509

IBT No.: 601-04930

Concentration: Undiluted

Classification: Moderately

Acute Dermal LD₅₀ = 298.0 mg/kg

Toxic

95% Confidence Limit of LD₅₀ = 220.7 - 402.3 mg/kg

Dose Level (mg/kg)	Animal Number and Sex	Individual Body Weights (kg)			Number Dead / Number Tested	Percent Dead
		0	Test Day Number: 7	14		
118.5	1-M*	3.00	3.26	3.20	0/4	0
	2-M	2.30	2.36	2.30		
	3-F*	2.46	2.94	3.06		
	4-F	2.38	2.22	2.36		
177.8	5-M*	2.44	(6-22 hours)	-	2/4	50
	6-M	2.54	(6 days)	-		
	7-F*	2.38	1.78	2.04		
	8-F	2.74	2.32	2.54		
266.7	9-M*	2.50	2.64	2.90	1/4	25
	10-M	2.94	2.46	2.88		
	11-F*	2.98	2.76	2.90		
	12-F	2.86	(3 days)	-		
400.0	13-M*	2.98	(3 days)	-	2/4	50
	14-M	2.70	(6-22 hours)	-		
	15-F*	2.98	2.84	3.10		
	16-F	2.48	2.32	2.54		
600.0	17-M*	2.82	(6-22 hours)	-	4/4	100
	18-M	2.94	(6-22 hours)	-		
	19-F*	3.02	(6-22 hours)	-		
	20-F	2.72	(6-22 hours)	-		

TABLE III continued

Acute Dermal Toxicity Study - Albino Rabbits

Mortality and Body Weight Data

Test Material: SN-1509

IBT No.: 601-04930

Concentration: Undiluted

Classification: Moderate

Acute Dermal LD₅₀ = 298.0 mg/kg

Toxic

95% Confidence Limits of LD₅₀ = 220.7 - 402.3 mg/kg

Dose Level (mg/kg)	Animal Number and Sex	Individual Body Weights (kg)			Number Dead / Number Tested	Percent Dead
		0	7	14		
900.0	21-M*	2.64	(6-22 hours)	-	4/4	100
	22-M	2.90	(6-22 hours)	-		
	23-F*	2.70	(6-22 hours)	-		
	24-F	2.90	(6-22 hours)	-		
3,000	25-M*	2.80	(6-22 hours)	-	4/4	100
	26-M	2.50	(6 hours)	-		
	27-F*	2.52	(6-22 hours)	-		
	28-F	2.50	(6 hours)	-		

Note: Figures in parentheses indicate time of death.

* Skin at the application site was abraded.

2. Reactions

The unusual behavioral reactions exhibited by the rabbits following dermal exposure to SN-1509 are presented in Table IV.

Local skin reactions at the end of the 24-hour contact period were characterized by beet red erythema, severe edema (area raised more than 1 mm), and second and focal third degree burns. At seven days second and third degree chemical burns and subdermal hemorrhages were noted. At fourteen days necrosis was observed.

Necropsy examination of the animals that died revealed hydroperitoneum at the 900.0 and 3,000 mg/kg dose levels. No other gross pathologic alterations were noted other than the dermal change as described.

TABLE IV

Acute Dermal Toxicity Study - Albino Rabbits

Summary of Reactions

Test Material: SN-1509
 Concentration: Undiluted

IBT No.: 601-04930

Dose Level (mg/kg)	Reaction	Time of Onset Following Dose Administration	Duration of Reaction	Time of Death Following Dose Administration
118.5	None	-	-	-
177.8	Hypoactivity Muscular weakness	6-22 hours 6-22 hours	5 days 5 days	6 hours-6 days
266.7	Hypoactivity Muscular weakness Loss of righting reflex Hypothermia Mydriasis	6-22 hours 6-22 hours 6-22 hours 6-22 hours 6-22 hours	5 days 2 days 2 days 2 days 2 days	3 days
400.0	Hypoactivity Muscular weakness Loss of righting reflex Hypothermia Mydriasis	5 hours 5 hours 5 hours 5 hours 5 hours	5 days 3 days 3 days 3 days 3 days	6 hours-3 days

TABLE IV continued

Acute Dermal Toxicity Study - Albino Rabbits

Summary of Reactions

Test Material: SN-1509

IBT No.: 601-04930

Dose Level (mg/kg)	Reaction	Time of Onset Following Dose Administration	Duration of Reaction	Time of Death Following Dose Administration
600.0, 900.0 and 3,000	Hypoactivity	5 hours	Until death	6-22 hours
	Muscular weakness	5 hours		
	Loss of righting reflex	5 hours		
	Hypothermia	5 hours		
	Mydriasis	5 hours		

C. Eye Irritation Test - Albino Rabbits

The results of the eye irritation test are presented in Table V.

TABLE V continued

Eye Irritation Test - Albino Rabbits

Results

Test Material: SN-1509

IBT No.: 601-04930

Tissue	Rabbit Number	1		24		72		7		14	
		Minute	Hour	Hours	Hours	Hours	Days	Days	Days		
Cornea (D-A)	5	20 (1-4),E	20 (1-4),E	20 (1-4)	80 (4-4),C,Y	80 (4-4),C	80 (4-4),C	80 (4-4),C	80 (4-4),C	80 (4-4),U,V	80 (4-4),U,V
Iris	5	5	5	10	10	10	10	10	10	10	10
Conjunctiva (R-S-D)		12 (2-1-3)	18 (2-4-3)	20 (3-4-3),H	20 (3-4-3),B,H	20 (3-4-3),H	16 (2-4-2)				
Total		37	43	50	110	110	110	110	110	106	
Cornea (D-A)	6	20 (1-4),E	20 (1-4),E	20 (1-4)	20 (1-4)	40 (2-4),P,V	80 (4-4),U,V	80 (4-4),U,V	80 (4-4),U,V	80 (4-4),U,V	80 (4-4),U,V
Iris	5	5	5	10	10	10	10	10	10	10	10
Conjunctiva (R-S-D)		12 (2-1-3)	18 (2-4-3)	20 (3-4-3),H	20 (3-4-3),H	20 (3-4-3),H	20 (3-4-3),H	20 (3-4-3),H	20 (3-4-3),H	16 (2-4-2)	16 (2-4-2)
Total		37	43	50	50	70	70	70	70	106	106

Averages

Cornea	20.0	20.0	20.0	50.0	53.3	70.0
Iris	5.0	5.0	10.0	10.0	10.0	10.0
Conjunctiva	12.0	18.0	20.0	20.0	19.0	16.7
Total	37.0	43.0	50.0	80.0	82.3	96.7

Cornea:

D = Density

A = Area

Corneal Score = D x A x 5

Maximum Score = 80

Iris:

Iris Score = Value x 5

Maximum Score = 10

Conjunctiva:

R = Redness

S = Swelling

D = Discharge

Conjunctival Score = (R+S+D) x 2

Maximum Score = 20

B = Chemical burn

C = Corrosion

E = Epithelial sloughing

H = Hemorrhages

P = Blister

U = Ulceration

V = Vascularization

Y = Hypopyon

TABLE V

Eye Irritation Test - Albino Rabbits

Results

Test Material: SN-1509
 Form Administered: 0.1 ml, Undiluted
 Special Instructions: Unwashed Eyes

IBT No.: 601-04930
 Descriptive Rating: Extremely Irritating
 (96.7/110)

Tissue	Rabbit Number	1		24		72		7		14	
		Minute	Hour	Hours	Hours	Hours	Days	Days	Days		
Cornea (D-A)	1	20 (1-4),E	20 (1-4),E	20 (1-4)	80 (4-4),U,Y	80 (4-4),U,V,Y	80 (4-4),C				
		5	5	10	10	10					
Conjunctiva (R-S-D)		12 (2-1-3)	18 (2-4-3)	20 (3-4-3),H	20 (3-4-3),F,H	20 (3-4-3),H	20 (3-4-3),H				
		37	43	50	110	110					
Total											110
Cornea (D-A)	2	20 (1-4),E	20 (1-4),E	20 (1-4)	40 (2-4),Y	40 (2-4),P,V,Y	60 (3-4),U,V,Y				
		5	5	10	10	10					
Iris		12 (2-1-3)	18 (2-4-3)	20 (3-4-3),H	20 (3-4-3),H	18 (3-4-2),H	18 (3-4-2)				
		37	43	50	70	68					
Total											88
Cornea (D-A)	3	20 (1-4),E	20 (1-4),E	20 (1-4)	40 (2-4),Y	40 (2-4),V,Y	40 (2-4),V				
		5	5	10	10	10					
Iris		12 (2-1-3)	18 (2-4-3)	20 (3-4-3),H	20 (3-4-3),H	20 (3-4-3),H	6 (2-1-0)				
		37	43	50	70	70					
Total											56
Cornea (D-A)	4	20 (1-4),E	20 (1-4),E	20 (1-4)	40 (2-4),Y	40 (2-4),P,V,Y	80 (4-4),C				
		5	5	10	10	10					
Iris		12 (2-1-3)	18 (2-4-3)	20 (3-4-3),H	20 (3-4-3),B,H	16 (3-3-2),B,H	20 (3-4-3)				
		37	43	50	70	66					
Total											110

D. Primary Skin Irritation Test - Albino Rabbits

The results of the primary skin irritation test are presented in Table VI.

TABLE VI

Primary Skin Irritation Test - Albino Rabbits

Results

Test Material: SN-1509

IBT No.: 601-04930

Form Administered: 0.5 ml, Undiluted

Descriptive Rating: Extremely Irritating

Special Instructions: 24-Hour Exposure

(8.0/8.0)

Period, Occluded Sites

Animal Number	Irritation Scores for Abraded Skin Sites At:				Irritation Scores for Intact Skin Sites At:			
	24 Hours		72 Hours		24 Hours		72 Hours	
	Er.	Ed.	Er.	Ed.	Er.	Ed.	Er.	Ed.
1	B,SH	-	B,SH	-	B,SH	-	B,SH	-
2	B,SH	-	B,SH	-	B,SH	-	B,SH	-
3	B,SH	-	B,SH	-	B,SH	-	B,SH	-
4	B,SH	-	B,SH	-	B,SH	-	B,SH	-
5	B,SH	-	B,SH	-	B,SH	-	B,SH	-
6	B,SH	-	B,SH	-	B,SH	-	B,SH	-
Mean	4.0	4.0	4.0	4.0	4.0	4.0	4.0	4.0

Subtotal 16.0

16.0

Primary Irritation Score = 8.0

Key:

Er. = Erythema

Ed. = Edema

B = Third degree chemical burn (will result in fibrosis)

SH = Subdermal hemorrhage

Note: Sites with third degree chemical burns were given maximum irritation scores of 4 for both erythema and edema to obtain a primary irritation score.

V. Appendix

The detailed investigational procedures employed in these studies are presented in the following pages.

ACUTE ORAL TOXICITY STUDY - ALBINO RATS

Young albino rats derived from Sprague-Dawley stock were used as test animals. All animals were kept under observation for five days prior to experimental use, during which period they were checked for general health and suitability as test animals. The animals were housed in stock cages and were permitted a standard laboratory diet plus water ad libitum, except during the 16-hour period immediately prior to oral intubation when food was withheld.

Initial screening was conducted in order to determine the general level of toxicity of the test material. Selected groups of albino rats were administered the test material at several dose levels. All doses were administered directly into the stomach of the rats using a hypodermic syringe equipped with a ball-tipped intubating needle.

After oral administration of the test material, the rats were housed individually in suspended, wire-mesh cages and observed for the following 14 days. Initial and final body weights, mortalities, and reactions were recorded. A necropsy examination was conducted on all animals.

At the end of the observation period, the acute oral median lethal dose (LD₅₀) of the test material was calculated, if possible, using the techniques of Litchfield and Wilcoxon*. The test material was then assigned a classification in accordance with Harold C. Hodge**. The classification system is presented in the following Table.

* Litchfield, J. T. Jr., and Wilcoxon, F., "A Simplified Method of Evaluating Dose-Effect Experiments," J. Pharm. & Exp. Ther. 96, 99 (1949).

** Hodge, Harold C., "The LD₅₀ and its value", American Perfumer and Cosmetics 80, 57 (1965).

TABLE

Acute Oral Toxicity Study - Albino Rats

Classification of Test Materials
Based on Acute Oral LD₅₀

Acute Oral LD ₅₀ (Range of Values)	Classification	Probable lethal dose for a 70 kg man in commonly used measures
Less than 5 mg/kg	Extremely toxic	a taste (less than 7 drops)
5 - 50 mg/kg	Highly toxic	between 7 drops and 1 teaspoonful
50 - 500 mg/kg	Moderately toxic	between 1 teaspoonful and 1 ounce
500 - 5,000 mg/kg	Slightly toxic	between 1 ounce and 1 pint or 1 pound
5,000 - 15,000 mg/kg	Practically non-toxic	between 1 pint and 1 quart
Greater than 15,000 mg/kg	Relatively harmless	more than 1 quart

ACUTE DERMAL TOXICITY STUDY - ALBINO RABBITS

Young adult albino rabbits of the New Zealand strain were used as test animals. All rabbits had been maintained under observation in the laboratory for at least seven days prior to testing. During the pre-test period, the animals were examined with respect to their general health and suitability as test animals. The rabbits were housed individually in suspended, wire-bottomed cages and maintained on a standard laboratory ration. Food and water were offered ad libitum.

Twenty-four hours prior to the dermal applications, the backs of the rabbits were shaved free of hair with electric clippers. The shaved area on each animal constituted about 30 percent of the total body surface area. The animals were then returned to their cages to await testing on the following day. The 24-hour waiting period allowed recovery of the stratum corneum from the disturbance which accompanied the close-clipping procedure and permitted healing of any microscopic abrasions possibly produced during the process.

The test material was applied at the highest reasonable dose level. The test site was covered by wrapping the trunk of the animal with impervious plastic sheeting which was securely taped in place. This plastic wrap insured close contact of the epidermis and test material. To prevent oral ingestion of the test material, each animal was fitted with a light-weight, flexible plastic collar which was worn throughout the observation period.

The test material remained in contact with the skin for 24 hours. At the end of this period, the plastic sheeting and all residual test material were removed. The test sites were examined for local skin reactions and the animals were returned to their cages. Observations for mortality, local skin reactions, and behavioral abnormalities were continued for a total of 14 days following the skin applications. Initial, 7 and 14-day body weights were recorded. A necropsy examination was conducted on all animals.

In the case of significant mortality following the initial study, additional experiments were conducted at lower dose levels in order to obtain data sufficient to calculate the acute dermal median lethal dose (LD_{50}), if possible, using the techniques of Litchfield and Wilcoxon*. The test material was then assigned a classification. The classification system is presented in the following Table.

* Litchfield, J. T. Jr., and Wilcoxon, F., "A Simplified Method of Evaluating Dose-Effect Experiments," J. Pharm. & Exp. Ther. 96, 99 (1949).

TABLE

Acute Dermal Toxicity Study - Albino Rabbits

Classification of Test Materials
Based on Acute Dermal LD₅₀

Acute Dermal LD ₅₀ (Range of Values)	Classification	Probable lethal dose for a 70 kg man in commonly used measures
Less than 20 mg/kg	Extremely toxic	approximately 30 drops
20 - 200 mg/kg	Highly toxic	between 30 drops and 4 teaspoonfuls
200 - 500 mg/kg	Moderately toxic	between 4 teaspoonfuls and 1 ounce
500 - 3,000 mg/kg	Slightly toxic	between 1 ounce and 1 pint or 1 pound
3,000 - 10,000 mg/kg	Practically non-toxic	between 1 pint and 1 quart
Greater than 10,000 mg/kg	Relatively harmless	more than 1 quart

EYE IRRITATION TEST - ALBINO RABBITS

Young albino rabbits of the New Zealand strain were used to evaluate the eye irritating properties of the test material. The test method was patterned after that of Draize et al.*

The test material was instilled into the conjunctival sac of the right eye of each rabbit. The left eye of each animal served as a control. At each scoring interval the cornea, iris, and palpebral conjunctiva were examined and graded for irritation and injury according to a standard scoring system*. The maximum possible score at any one examination and scoring period is 110 points, which indicates maximal irritation and damage to all three ocular tissues. Zero score indicates no irritation. The scoring system is presented in Table A. In this scoring system, special emphasis is placed upon irritation or damage to the cornea, while less emphasis is placed upon damage to the iris and conjunctiva.

After the completion of the test, the scores were analyzed, and a descriptive eye irritation rating was assigned to the test material. The criteria used for assignment of the descriptive rating are the frequency, the extent, and the persistence of irritation or damage which occur to the three ocular tissues.

* Draize, John H., Woodard, Geoffrey, and Calvery, Herbert O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther. 82, 377 (1944).

TABLE A

Eye Irritation Test - Albino Rabbits

Scale of Weighted Scores for
Grading the Severity of Ocular Lesions

Ocular Tissues	Description	Grading	
Cornea	<u>Opacity (A)</u>		
	Opacity - Degree of density (area which is most dense is taken for reading). Scattered or diffuse area, details of iris clearly visible.	1	
	Easily discernible translucent areas, details of iris slightly obscured.	2	
	Opalescent areas, no details of iris visible, size of pupil barely discernible.	3	
	Opaque, iris invisible.	4	
	<u>Area of Cornea Involved (B)</u>		
	One quarter (or less) but not zero.	1	
	Greater than one-quarter but less than one-half.	2	
	Greater than one-half but less than three-quarters.	3	
	Greater than three-quarters, up to whole area.	4	
	Score equals A x B x 5	Total maximum = 80	
	Iris	<u>Values (A)</u>	
		Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or a combination of any thereof), iris still reacting to light (sluggish reaction is positive).	1
		No reaction to light, hemorrhage, gross destruction (any or all of these).	2
Score equals A x 5		Total maximum = 10	

TABLE A continued

Eye Irritation Test - Albino Rabbits

Scale of Weighted Scores for
Grading the Severity of Ocular Lesions

Ocular Tissues	Description	Grading
Conjunctiva	<u>Redness (A)</u>	
	Redness (refers to palpebral conjunctiva only). Vessels definitely injected above normal.	1
	More diffuse, deeper crimson red, individual vessels not easily discernible.	2
	Diffuse beefy red.	3
	<u>Chemosis (B)</u>	
	Any swelling above normal (includes nictitating membrane).	1
	Obvious swelling with partial eversion of the lids.	2
	Swelling with lids about half-closed.	3
	Swelling with lids about half-closed to completely closed.	4
	<u>Discharge (C)</u>	
	Any amount different from normal (does not include small amount observed in inner canthus of normal animals).	1
	Discharge with moistening of the lids and hairs just adjacent to the lids.	2
Discharge with moistening of the lids and hairs and considerable area around eye.	3	
Score (A + B + C) x 2		Total maximum = 20

Note: The maximum total score is the sum of all scores obtained from the cornea, iris, and conjunctiva.

The rating is obtained by selecting the maximum mean irritation score at one, 24, or 72 hours after instillation. If the rate of dissipation of injury does not meet the requirements defined for the descriptive rating appropriate for a particular numerical score, the descriptive rating is raised by one or more levels. The rating system is presented in Table B.

TABLE B

Eye Irritation Test - Albino Rabbits

Classification of Test Materials
Based on Eye Irritation Properties

Rating	Range	Definition
Non-Irritating	0.0 - 0.5	To maintain this rating, all scores at the 24-hour reading must be zero; otherwise, increase rating one level.
Practically Non-Irritating	Greater than 0.5 - 2.5	To maintain this rating, all scores at the 24-hour reading must be zero; otherwise increase rating one level.
Minimally Irritating	Greater than 2.5 - 15.0	To maintain this rating, all scores at the 72-hour reading must be zero; otherwise, increase rating one level.
Mildly Irritating	Greater than 15.0 - 25.0	To maintain this rating, all scores at the 7-day reading must be zero; otherwise, increase rating one level.
Moderately Irritating	Greater than 25.0 - 50.0	To maintain this rating, scores at 7 days must be less than or equal to 10 for 60% or more of the animals. Also, mean 7-day score must be less than or equal to 20. If 7-day mean score is less than or equal to 20 but less than 60% of animals show scores less than 10, then no animal among those showing scores greater than 10 can exceed a score of 30 if rating is to be maintained; otherwise, increase rating one level.
Severely Irritating	Greater than 50.0 - 80.0	To maintain this rating, scores at 7 days must be less than or equal to 30 for 60% or more of the animals. Also, mean 7-day score must be less than or equal to 40. If 7-day mean score is less than or equal to 40 but less than 60% of the animals show scores less than or equal to 30, then no animal among those showing scores greater than 30 can exceed a score of 60 if rating is to be maintained; otherwise, increase rating one level.
Extremely Irritating	Greater than 80.0 - 110.0	

PRIMARY SKIN IRRITATION TEST - ALBINO RABBITS

Young albino rabbits of the New Zealand strain were used in the evaluation of the primary skin irritating properties of the test material. The test procedure was modeled after that of Draize et al.*

Prior to the application of the test material, the hair was clipped from the back and flanks of each rabbit. Two test sites located lateral to the midline of the back approximately ten centimeters apart were selected. One of the two sites was abraded by making four epidermal incisions, two perpendicular to the other two, while the other test site remained intact.

The test material was applied to each of the test sites on each rabbit and occluded with gauze patches which were secured with masking tape. The trunk of each animal was then wrapped with impervious plastic sheeting. The wrap held the patches in position and retarded evaporation of the test material during the 24-hour exposure period.

At the end of 24 hours, the plastic wrappings, patches, and all residual test material were removed. The intact and abraded test sites were examined and scored separately for erythema and edema on a graded scale of 0 to 4. After 72 hours, the sites were again examined and scored.

* Draize, John H., Woodard, Geoffrey, and Calvery, Herbert O., "Methods for the Study of Irritation and Toxicity of Substances Applied Topically to the Skin and Mucous Membranes," J. Pharm. & Exp. Ther. 82, 377 (1944).

In evaluating the average irritation present, the mean scores for erythema and edema of the intact test sites after 24 and 72 hours were added. Similarly, the mean scores for erythema and edema of the abraded test sites after 24 and 72 hours were added. These two values were totaled and divided by four to obtain the mean primary irritation score. The scoring criteria for erythema and edema are shown in the following Table.

The following grading system was used to arrive at a descriptive primary skin irritation rating:

<u>Mean Primary Irritation Score</u> <u>(Range of Values)</u>	<u>Descriptive Rating</u>
0	Non-Irritating
0.1 - 0.5	Minimally Irritating
0.6 - 1.5	Slightly Irritating
1.6 - 3.0	Mildly Irritating
3.1 - 5.0	Moderately Irritating
5.1 - 6.5	Severely Irritating
6.6 - 8.0	Extremely Irritating

TABLE
 Primary Skin Irritation Test - Albino Rabbits
 Scoring Criteria for Skin Reactions

Reactions	Description	Score
Erythema	Barely perceptible (Edges of area not defined)	1
	Pale red in color and area definable	2
	Definite red in color and area well defined	3
	Beet or crimson red in color	4
Edema	Barely perceptible. (Edges of area not defined)	1
	Area definable but not raised more than 1 mm	2
	Area well defined and raised approximately 1 mm	3
	Area raised more than 1 mm	4
Injury In Depth	Escharosis, Necrosis	8
	Maximum Primary Irritation Score =	8



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAR 30 1995

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Sincerely,

Terry R. O'Bryan
Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12190A



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NON-CAP

CAP

Submission number: 12190A

TSCA Inventory:

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Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

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CECATS DATA: Submission # 8EHQ 0992-12190 SEQ. A
 TYPE: INT. SUPP FLWP
 SUBMITTER NAME: Rhone-Poulenc Inc.

SECONDARY ACTIONS:
 0400 (NO) ACTION REPORT ID
 0402 STUDIES PLANNED (ADMIN HMA)
 0403 NOTIFICATION (H WORK) REPORTING
 0404 LABELS/MSDS CHANGES
 0405 PROCESS/AND/OR CHANGES
 0406 APP. USE DISCONTINUED
 0407 PRODUCTION DISCONTINUED
 0408 CONFIDENTIAL

INFORMATION REQUESTED: FLWP DATE
 0501 NO INFO REQUESTED
 0502 INFO REQUESTED (TECH)
 0503 INFO REQUESTED (VOL ACTIONS)
 0504 INFO REQUESTED (REPORTING RATIONAL.F)
 DISPOSITION:
 0639 REFER TO CHEMICAL SCREENING
 0678 CAP NOTICE

SUB. DATE: 09/04/92 OTS DATE: 09/21/92 CSRAD DATE: 01/26/95

CHEMICAL NAME: _____
 CAS# 818-61-1

INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C	INFORMATION TYPE:	P F C
0201 ONCO (HUMAN)	01 02 04	EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL. TRANS (IN VITRO)	01 02 04	HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEM/PHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	ECOAQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	ENV. OCCUREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	EMER INCI OF ENV CONTAM	01 02 04	0247 DNA DAM/REPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	RESPONSE REQEST DELAY	01 02 04	0248 PROD/USE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	PROD/COMP/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	REPORTING RATIONALE	01 02 04	OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	ALLERG (HUMAN)	01 02 04		
0213 SUB ACUTE TOX. (ANIMAL)	01 02 04	ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	METAB/PHARMACO (HUMAN)	01 02 04		

TRIAJE DATA: NON-CL INVENTORY YES
 CAS SR NO
 ONGOING REVIEW: YES (DROP/REFER) NO (CONTINUE)
 SPECIES: RBT RAT
 TOXICOLOGICAL CONCERN: LOW MED HIGH
 USE: _____ PRODUCTION: _____

> <ID NUMBER>
8(e)-12190A

> <TOX CONCERN>
H/M

> <COMMENT>

SKIN IRRITATION IN RABBITS IS HIGH CONCERN. WHEN ANIMALS WERE ADMINISTERED 0.5 ML OF TEST MATERIAL A PRIMARY IRRITATION SCORE OF 8.0 RESULTED. THE TEST MATERIAL WAS DETERMINED TO BE EXTREMELY IRRITATING CAUSING THIRD DEGREE CHEMICAL BURNS THAT WILL RESULT IN FIBROSIS AND SUBDERMAL HEMORRHAGES. EYE IRRITATION IN RABBITS IS HIGH CONCERN. THE TEST MATERIAL WAS FOUND TO BE EXTREMELY IRRITATING TO UNWASHED EYES CAUSING THIRD DEGREE BURNS AND SUBDERMAL HEMORRHAGES. CLINICAL OBSERVATIONS INCLUDED CONJUNCTIVAL REDNESS, SWELLING, AND DISCHARGE; EPITHELIAL SLOUGHING, HYPOPYON, IRRITATION OF THE IRIS AND CORROSION OF THE CORNEA.

ACUTE DERMAL TOXICITY IN RABBITS IS MEDIUM CONCERN WITH AN LD50 OF 298 MG/KG. DOSE (MG/KG) AND MORTALITY: 118.5 (0/4), 177.8 (2/2 M, 0/2 F), 266.7 (0/2 M, 1/2 F), 400 (2/2 M, 0/2 F), 600 (4/4), 900 (4/4) AND 3000 (4/4). THE TEST MATERIAL CAUSED SECOND AND THIRD DEGREE CHEMICAL BURNS, SUBDERMAL HEMORRHAGES, NECROSIS, BEET RED ERYTHEMA, AND SEVERE EDEMA. CLINICAL OBSERVATIONS INCLUDED HYPOACTIVITY, MUSCULAR WEAKNESS, LOSS OF RIGHTING REFLEX, HYPOTHERMIA, AND MYDRIASIS. NECROPSY OF DECEDENTS REVEALED HYDROPERITONEUM AT THE 900 AND 3000 MG/KG DOSE LEVELS.

ACUTE ORAL TOXICITY IN RATS IS MEDIUM CONCERN WITH AN LD50 OF 548 MG/KG. DOSE (MG/KG) AND MORTALITY: 266.7 (0/4), 400 (0/4), 600 (2/2 M, 1/2 F), AND 900 (4/4). CLINICAL OBSERVATIONS INCLUDED HYPOACTIVITY, RUFFLED FUR, LABORED BREATHING, AND MUSCULAR WEAKNESS. NECROPSY OF DECEDENTS REVEALED HEMORRHAGES IN THE GI TRACT.