RHÔNE-POULENC

Contains No CBI

92 SEP 22 AM 9:42

8EHQ-92-12104
INIT
8892001034 4

RHÔNE-POULENC INC.
CN 7500, CRANBURY, NJ 08512-7500
TELEPHONE: (609) 395-8300

September 4, 1992

CERTIFIED MAIL
RETURN RECEIPT REQUESTED
P 640 082 580

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 - 0244

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:	Pentaerythritol triacrylate (PETA)
CAS Registry No:	3524-68-3
CAS Registry Name:	2-Propenoic acid, 2-(hydroxymethyl)-2-[((1-oxo-2-propenyl)oxy)methyl]-1,3-propanediyl ester

The title of the enclosed report is:

Acute Toxicity Studies With Peta (Pentaerythritol Triacrylate) SN-1718

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

The test material was found to be severely irritating to the skin of rabbits in the dermal toxicity study. Although the dermal LD50 was greater than 2000 mg/kg, well defined erythema, severe edema, second degree burns, and subdermal hemorrhages were observed at 24 hours and escharosis was observed at day 14. In the primary skin irritation study, the test material was classified as moderately irritating although second degree burns, blanching, and subdermal hemorrhage were observed at 72 hours at abraded skin sites.

3/10/95

(2)

The eye irritation test revealed the test material to be extremely irritating to the eyes of rabbits. At day 14, chemical burns and vascularization were observed in all animals.

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

One TSCA Section 8(e) notice was made on this chemical. This notice was submitted to EPA on August 6, 1982 by Celanese, but we are unable to find a Document Control Number in our files for the submission. RPI is also submitting other studies on this material under the CAP agreement; see RP CAP Report Nos. RPS-0184, RPS-0185, and RPS-0190.

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.

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

CEMjr/mm
Enclosures

Industrial BIO-TEST Laboratories, Inc.
1810 FRONTAGE ROAD
NORTHBROOK, ILLINOIS 60062

CAP ID No. S-LT-PIN-0187
Reviewed for Sec. 8 (e)
Compliance Program
On 5/26/82 By

REPORT TO

CELANESE CORPORATION

ACUTE TOXICITY STUDIES WITH PETA (PENTAERYTHRITOL TRIACRYLATE) SN-1718

P.O. NO. 045-2940-75

MARCH 11, 1976

IBT NO. 601-08135

REPORT TO

CELANESE CORPORATION

ACUTE TOXICITY STUDIES WITH
PETA (PENTAERYTHRITOL TRIACRYLATE) SN-1718

P.O. NO. 045-2940-75

MARCH 11, 1976

IBT NO. 601-08135

I. Introduction

At the request of the Celanese Corporation, the following studies were conducted with a thick white liquid identified as PETA (pentaerythritol triacrylate) SN-1718:

Acute Oral Toxicity Study - Albino Rats

Acute Dermal Toxicity Study - Albino Rabbits

Eye Irritation Test - Albino Rabbits

Primary Skin Irritation Test - Albino Rabbits

(5)

II. Summary

The results of the acute toxicity studies with PETA (pentaerythritol triacrylate) SN-1718 are summarized below:

Test	Results
Acute Oral Toxicity Study - Albino Rats	Slightly Toxic LD_{50} = 1,830 mg/kg Standard Deviation of LD_{50} = ± 284.4 mg/kg
Acute Dermal Toxicity Study - Albino Rabbits	Slightly Toxic LD_{50} >2,000 mg/kg
Eye Irritation Test - Albino Rabbits	Extremely Irritating (109.2/110.0)
Primary Skin Irritation Test - Albino Rabbits	Moderately Irritating (4.7/8.0)

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

Report prepared by:

Glenn E. Trzyna, B.A.
Technician
Acute Toxicity

Helfried Paa
Assistant Group Leader
Acute Toxicity

Report approved by:

C. W. Mastri, B.S.
Section Head, Acute Toxicity

Florence K. Kinoshita, Ph.D.
Technical Manager, Toxicology

M. L. Keplinger, Ph.D.
Manager, Toxicology

trm

III. Results

A. Acute Oral Toxicity Study - Albino Rats

1. Mortality and Body Weights

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

2. Reactions and Pathology

The pharmacotoxic symptoms exhibited by the animals post-oral administration of PETA (pentaerythritol triacrylate) SN-1718 are presented in Table II.

Necropsy examination of the animals that died revealed gastroenteritis. In addition, animal No. 3-F and 10-M revealed gastrointestinal hemorrhages. Examination of the survivors did not reveal any gross pathologic alterations.

TABLE I

Acute Oral Toxicity Study - Albino Rats

Mortality and Body Weight Data

IBT No.: 601-08135
Test Material: PETA (pentaerythritol triacrylate) SN-1718
Form Administered: Undiluted

Classification: Slightly Toxic
Acute Oral LD_{50} = 1,830 mg/kg
Standard Deviation of LD_{50} = ± 284.4 mg/kg

Dose Level (mg/kg)	Animal Number	Individual Body Weights (g) Test Day Number 0	14	Number Dead / Number Tested	Percent Dead
1,350	1-M	248	336	1/4	25
	2-M	246	324		
	3-F	184	(2 days)		
	4-F	204	228		
2,025	5-M	208	328	2/4	50
	6-M	200	326		
	7-F	168	(6-22 hours)		
	8-F	166	(6-22 hours)		
3,038	9-M	214	(6-22 hours)	4/4	100
	10-M	210	(1 day)		
	11-F	162	(6-22 hours)		
	12-F	156	(6-22 hours)		
4,556	13-M	242	(6-22 hours)	4/4	100
	14-M	269	(6-22 hours)		
	15-F	200	(6-22 hours)		
	16-F	208	(6-22 hours)		
15,380	17-M	254	(2 hours)	4/4	100
	18-M	238	(6-22 hours)		
	19-F	190	(6-22 hours)		
	20-F	194	(2 hours)		

Note: Figures in parentheses indicate time of death.

TABLE II

Acute Oral Toxicity Study - Albino Rats

Summary of Reactions

Test Material: PETA (pentaerythritol triacrylate) SN-1718
Form Administered: Undiluted

	Dose Levels (mg/kg)									
	1,350		2,025		3,038		4,556		15,380	
Reactions	O	R	O	R	O	R	O	R	O	R
Hypoactivity	5 M	2 D	5 M	2 D	5 M	N	5 M	N	5 M	N
Salivation	-	-	-	-	-	-	10 M	N	10 M	N
Diarrhea	1 H	2 D	30 M	2 D	30 M	N	15 M	N	15 M	N
Muscular weakness	6-22 H	2 D	6-22 H	2 D	6-22 H	N	-	-	2 H	N
Labored breathing	6-22 H	2 D	6-22 H	2 D	6-22 H	N	-	-	2 H	N
Prostration	-	-	-	-	-	-	-	-	2 H	N
Ptosis	6-22 H	2 D	6-22 H	2 D	6-22 H	N	-	-	-	-

O = Onset
R = Recovery
- = No Reaction

D = Days
H = Hours

M = Minutes
N = No Recovery

B. Acute Dermal Toxicity Study - Albino Rabbits

1. Mortality and Body Weights

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

2. Reactions and Pathology

No pharmacotoxic symptoms were exhibited by the rabbits following dermal exposure to PETA (pentaerythritol triacrylate) SN-1718.

The test material was severely irritating to the skin of the albino rabbit. Skin changes at 24 hours were characterized by pale red to red, well-defined erythema, moderate to severe edema, second degree burns and subdermal hemorrhages. Pale red to red, well-defined erythema, second degree burns, escharosis, wrinkling and fissuring were noted at 7 days. Escharosis was observed at 14 days.

Necropsy examination revealed mottled kidneys in rabbit Nos. 2-M, 3-F and 4-F. No other gross pathologic alterations were noted except for the local skin changes as previously described.

TABLE III

Acute Dermal Toxicity Study - Albino Rabbits

Mortality and Body Weight Data

IBT No.: 601-08135
Test Material: PETA (pentaerythritol triacrylate) SN-1718
Form Administered: Undiluted

Classification: Slightly Toxic
Acute Dermal LD_{50} >2,000 mg/

Dose Level (mg/kg)	Animal Number and Sex	Individual Body Weights (kg) Test Day Number: 0	7	14	Number Dead / Number Tested	Percent Dead
2,000	1-M*	2.72	2.80	3.04	0/4	0
	2-M	3.00	3.06	3.16		
	3-F*	2.86	2.86	2.96		
	4-F	2.72	2.84	3.00		

* The skin at the site of application was abraded.

C. Eye Irritation Test - Albino Rabbits

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

TABLE IV

Eye Irritation Test - Albino Rabbits

Results

IBT No.: 601-08135
Test Material: PETA (pentaerythritol triacrylate) SN-1718
Form Administered: Instillation (0.1 ml, undiluted)
Special Instructions: Unwashed eyes

Classification: Extremely Irritating
Maximum Mean
Irritation Score: 109.2/110.0

Tissue	Rabbit Number	1 Hour	24 Hours	48 Hours	72 Hours	7 Days	14 Days
Cornea (D-A)	1	*	20 (1-4)	40 (2-4)	40 (2-4)	60 (3-4), V, Y	80 (4-4), M, V
Iris		*	5	5	5	5	10
Conjunctiva (R-S-D)		16 (1-4-3)	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B	20 (3-4-3), B
Total		16	45	65	65	85	110
Cornea (D-A)	2	*	20 (1-4)	40 (2-4)	40 (2-4)	80 (4-4), U, V, Y	80 (4-4), M, V
Iris		*	5	5	5	10	10
Conjunctiva (R-S-D)		16 (1-4-3)	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B	20 (3-4-3), B
Total		16	45	65	65	110	110
Cornea (D-A)	3	*	20 (1-4)	40 (2-4)	40 (2-4)	80 (4-4), V, X, Y	80 (4-4), V, X
Iris		*	5	5	5	10	10
Conjunctiva (R-S-D)		16 (1-4-3)	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B	20 (3-4-3), B
Total		16	45	65	65	110	110
Cornea (D-A)	4	*	20 (1-4)	40 (2-4)	40 (2-4)	80 (4-4), V, Y	80 (4-4), M, V
Iris		*	5	5	5	10	10
Conjunctiva (R-S-D)		16 (1-4-3)	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B	20 (3-4-3), B
Total		16	45	65	65	110	110
Cornea (D-A)	5	*	20 (1-4)	40 (2-4)	40 (2-4)	80 (4-4), V, Y	80 (4-4), V, Y
Iris		*	5	5	5	10	10
Conjunctiva (R-S-D)		16 (1-4-3)	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B	20 (3-4-3), B
Total		16	45	65	65	110	110
Cornea (D-A)	6	*	20 (1-4)	40 (2-4)	40 (2-4)	60 (3-4), V, Y	80 (4-4), V, Y
Iris		*	5	5	5	5	5
Conjunctiva (R-S-D)		16 (1-4-3)	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B, H	20 (3-4-3), B	20 (3-4-3), B
Total		16	45	65	65	85	105
Averages							
Cornea		*	20.0	40.0	40.0	73.3	80.0
Iris		*	5.0	5.0	5.0	8.3	9.2
Conjunctiva		16.0	20.0	20.0	20.0	20.0	20.0
Total		16.0	45.0	65.0	65.0	101.6	109.2

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
H = Hemorrhages
U = Ulceration
V = Vascularization
Y = Hypopyon

X = Pannus
M = Descemetocele

* Extensive swelling to conjunctiva prevented evaluation at this interval.

D. Primary Skin Irritation Test - Albino Rabbits

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

TABLE V

Primary Skin Irritation Test - Albino Rabbits

Results

IBT No.: 601-08135
Test Material: PETA (pentaerythritol triacrylate) SN-1718
Form Administered: 0.5 ml, undiluted
Special Instructions: 24-hour exposure period, occluded sites

Classification: Moderately Irritating
Maximum Mean Irritation Score: 4.7/8.0

Animal Number	Irritation Scores for Abraded Skin Sites at: 24 Hours Er.	24 Hours Ed.	72 Hours Er.	72 Hours Ed.	Irritation Scores for Intact Skin Sites at: 24 Hours Er.	24 Hours Ed.	72 Hours Er.	72 Hours Ed.
1	2	2	2	0	2	2	2	0
2	2	1	1	0	1	0	1	0
3	3	4	SCB	-	3	2	2	1
4	2	2	SCB	-	2	0	1	0
5	3	4	B	-	3	4	B	-
6	4	4, SH	3	3, SH	3	4	3	2
Mean	2.7	2.8	3.0	2.5	2.3	2.0	2.2	1.2
Subtotal		11.0				7.7		

Primary Irritation Score = 4.7

Er. = Erythema
Ed. = Edema
SCB = Second degree chemical burn that will not result in fibrosis. Sites with second degree chemical burns were given maximum irritation scores of 4 for both erythema and edema to obtain a primary irritation score.
B = Third degree chemical burn that will result in fibrosis. Sites with third degree chemical burns were given maximum irritation scores of 4 for both erythema and edema to obtain a primary irritation score.
SH = Subdermal hemorrhage

IV. 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 stomachs 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 (LD_{50}) of the test material was calculated, if possible, using the techniques of Weil*, Thompson**, and Thompson and Weil***. The test material was then assigned a classification in accordance with Harold C. Hodge****. The classification system is presented in the following Table.

* Weil, Carrol S.: Tables for Convenient Calculation of Median-Effective Dose (LD_{50} or ED_{50}) and Instructions in Their Use. Biometrics, Sept. 1952.

** Thompson, William R.: Use of Moving Averages and Interpolation to Estimate Median-Effective Dose. Bact. Rev., Nov. 1947.

*** Thompson, William R. and Weil, Carrol S.: On the Construction of Tables for Moving Average Interpolation. Biometrics, March 1952.

**** Hodge, Harold C., "The LD_{50} 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 LD_{50}

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 determine the acute dermal median lethal dose (LD_{50}), if possible, using the techniques of Weil*, Thompson**, and Thompson and Weil*** The test material was then assigned a classification. The classification system is presented in the following Table.

* Weil, Carrol S.: Tables for Convenient Calculation of Median-Effective Dose (LD_{50} or ED_{50}) and Instructions in Their Use. Biometrics, Sept. 1952.

** Thompson, William R.: Use of Moving Averages and Interpolation to Estimate Median-Effective Dose. Bact. Rev., Nov. 1947.

*** Thompson, William R. and Weil, Carrol S.: On the Construction of Tables for Moving Average Interpolation. Biometrics, March 1952.

TABLE

Acute Dermal Toxicity Study - Albino Rabbits

Classification of Test Materials
Based on Acute Dermal LD_{50}

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	Opacity (D)	
	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
	Area of Cornea Involved (A)	
	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 D x A x 5 Total maximum = 80	
Iris	Values	
	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 value 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	Redness (R)	
	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
	Chemosis (S)	
	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
	Discharge (D)	
	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 (R + S + D) 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, 48 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 l
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 following grading system was used to arrive at a primary skin irritation classification:

Mean Primary Irritation Score (Range of Values)	Classification
0	Nonirritating
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

The scoring criteria for erythema and edema are shown in the following table:

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

Charles E. Moyer, Jr., Ph.D.
Director, Product Safety
Rhône-Poulenc Inc.
CN 7500
Cranberry, New Jersey 08512-7500

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

MAY 0 8 1995

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and **refer to the reverse side of this page for "EPA Information Requests"** .

All TSCA 8(e) submissions are placed in the public files unless confidentiality is claimed according to the procedures outlined in Part X of EPA's TSCA §8(e) policy statement (43 FR 11110, March 16, 1978). Confidential submissions received pursuant to the TSCA §8(e) Compliance Audit Program (CAP) should already contain information supporting confidentiality claims. This information is required and should be submitted if not done so previously. To substantiate claims, submit responses to the questions in the enclosure "Support Information for Confidentiality Claims". This same enclosure is used to support confidentiality claims for non-CAP submissions.

Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

Document Processing Center (7407)
Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12106A

Recycled/Recyclable
Printed with Soy/Canola Ink on paper that contains at least 50% recycled fiber

Triage of 8(e) Submissions

Date sent to triage: MAY 0 9 1995

NON-CAP (CAP)

Submission number: 12106A

TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: (0) 1 2 **pages** 1 2 **pages** 1 2 5

Notes:

Contractor reviewer : PR **Date:** 4/26/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0992 -12106 SEQ. A

TYPE (INT) SUPP FLWP

SUBMITTER NAME: Rhone - Poulenc Inc.

SUB. DATE: 09/04/92 OTS DATE: 09/22/92 CSRAD DATE: 03/10/95

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0401) NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

CHEMICAL NAME: PETA

CAS# 3524-68-3

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

ATOX

TRIAGE DATA:

NON-CBI INVENTORY
(YES)
CAS SR
NO
[illegible]

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RBT
RAT

TOXICOLOGICAL CONCERN:
LOW
(MED)
(HIGH)

USE:

PRODUCTION:

COMMENTS

-CPSS- 0927952113

0 0 0 0 0 0 0 0 0 0 0
> <ID NUMBER>
8(E)-12106A

> <TOX CONCERN>
H/M/L

> <COMMENT>
EYE IRRITATION IS HIGH CONCERN IN RABBITS. 6 ANIMALS WERE ADMINISTERED 0.1 ML OF UNDILUTED TEST MATERIAL. THE TEST MATERIAL WAS FOUND TO BE EXTREMELY IRRITATING WITH A MAXIMUM MEAN IRRITATION SCORE OF 109.2. CLINICAL OBSERVATIONS INCLUDED CORNEAL IRRITATION, IRITIS, AND CONJUNCTIVAL IRRITATION CONSISTING OF REDNESS, CHEMOSIS, SWELLING, CHEMICAL BURNS, HEMORRHAGES, ULCERATIONS, VASCULARIZATION, HYPOPYON, AND PANNUS.

PRIMARY SKIN IRRITATION IN RABBITS IS MEDIUM CONCERN. 6 ANIMALS WERE ADMINISTERED 0.5 ML OF UNDILUTED TEST MATERIAL. THE TEST MATERIAL WAS FOUND TO BE MODERATELY IRRITATING WITH A MAXIMUM MEAN IRRITATION SCORE OF 4.7. CLINICAL SIGNS INCLUDED ERYTHEMA, EDEMA, SECOND DEGREE BURNS, THIRD DEGREE BURNS THAT WILL RESULT IN FIBROSIS, AND SUBDERMAL HEMORRHAGE.

ACUTE DERMAL TOXICITY IN RABBITS IS LOW CONCERN BASED ON AN LD50 OF > 2000 MG/KG. 2000 MG/KG OF TEST MATERIAL WAS ADMINISTERED TO THE ABRADED SKIN OF 4 ANIMALS. CLINICAL OBSERVATIONS INCLUDED RED, WELL-DEFINED ERYTHEMA, MODERATE TO SEVERE EDEMA, SECOND DEGREE BURNS, SUBDERMAL HEMORRHAGES, ESCHAROSIS, WRINKLING, AND FISSURING. NECROPSY REVEALED MOTTLED KIDNEYS.

ACUTE ORAL TOXICITY IN RATS IS LOW CONCERN BASED ON AN LD50 OF 1830 MG/KG. DOSE (MG/KG) AND MORTALITY: 1350 (0/2 M, ½ F), 2025 (0/2 M, 2/2 F), 3038 (2/2 M , 2/2 F), 4556 (2/2 M, 2/2 F), AND 15380 (2/2 M, 2/2 F). CLINICAL SIGNS INCLUDED HYPOACTIVITY, SALIVATION, DIARRHEA, MUSCULAR WEAKNESS, LABORED BREATHING, PROSTRATION, AND PTOSIS. NECROPSY OF THE DECEDENTS REVEALED GASTROENTERITIS AND GI HEMORRHAGES.

$$$$