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September 4, 1992

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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 - 0195

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: Tripropylene glycol diacrylate
(Coded as C-178 in the report)

CAS Registry No: 42978-66-5

CAS Registry Name: 2 Propenoic acid, (1-methyl-1,2-ethanediyl)bis [oxy(methyl-2,1-ethanediyl)] ester

2/16/95

The title of the enclosed report is:

Ten-Day Dermal Toxicity Study in Rabbits

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

Test material was administered by application to abraded and intact skin of New Zealand White rabbits (5/sex/group) at 500 mg/kg/day (neat, in corn oil, or in acetone) for 10 days. Animals were allowed approximately a three-week recovery period after dosing to evaluate reversibility.

Dermal lesions were exhibited by animals in all treated groups. These lesions included blanching, eschar, epidermal scaling, fissuring, necrosis, sloughing, and thickening. Several of these lesions were noted throughout the reversibility period.

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

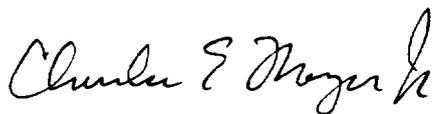
RPI has not previously submitted any TSCA Section 8(e) notices or premanufacture notification on the subject chemical substance.

RPI has submitted six other studies on this material under the CAP agreement; see RP CAP Report Nos. RPS-0191, RPS-0192, RPS-0193, RPS-0194, RPS-0196 and RPS-0274.

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-PCN-0169
Reviewed for Sec. 8 (e)
Compliance Program
On 10/24/91 By NA

TEN-DAY DERMAL TOXICITY STUDY IN RABBITS

C-178

FINAL REPORT

Submitted to

Celanese Corporation
New York, New York



HAZLETON

LABORATORIES AMERICA, INC.

9200 LEESBURG TURNPIKE, VIENNA, VIRGINIA 22180, U.S.A.

July 21, 1981



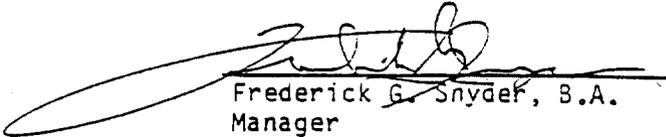
OFFICE OF QUALITY ASSURANCE

Project Title: Ten Day Dermal Toxicity Study in Rabbits

Project No.: 299-525

Quality Assurance review of the final report was conducted according to the procedures described in the standard operating procedures of the Report Review Section of the Office of Quality Assurance, and according to the general requirements of the Good Laboratory Practice regulations that were issued on December 22, 1978, by the Food and Drug Administration for compliance on and after June 20, 1979. The final report review was conducted and the findings were reported to management and to the study director on the following dates:

<u>Final Report Review</u>	<u>Findings Reported</u>	<u>Reviewer</u>
7/13-15/81	7/17/81	Congleton


Frederick G. Snyder, B.A.
Manager
Office of Quality Assurance



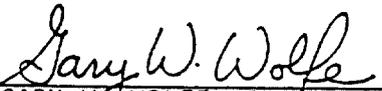
SUBJECT: Ten-Day Dermal Toxicity Study in Rabbits
Project No. 299-525

We, the undersigned, hereby declare that the work was performed under our supervision, according to the procedures herein described.

Study Director:


DAVID G. SEROTA, Ph.D.
Project Coordinator
Toxicology Department

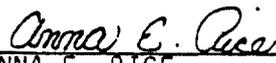
Laboratory Supervision:


GARY W. WOLFE, Ph.D.
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Pathology:


RICHARD W. VOELKER, D.V.M., Ph.D.
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HAZLETON
LABORATORIES AMERICA, INC.

SPONSOR: Celanese Corporation

DATE: July 21, 1981

MATERIAL: C-178

SUBJECT: FINAL REPORT
Ten-Day Dermal Toxicity Study in Rabbits
Project No. 299-525

SUMMARY

The dermal toxicity of C-178 was evaluated after repeated topical applications for ten consecutive days on the abraded and intact dorsal skin of four groups of New Zealand White rabbits (five/sex/group). The compound was applied at a dosage level of 500 mg/kg in each of the treated groups. The compound was applied undiluted to Group 2, in corn oil vehicle to Group 3, and in acetone vehicle to Group 4. The exposure area of three males and two females in each group was abraded prior to the first, third, sixth, and eighth doses. An additional group (Group 1) served as a control and was abraded in the same manner. Criteria used to evaluate for compound effect were mortality and moribundity, clinical observations, dermal responses, body weights, gross pathology, and histopathology.

One Group 4 female was found dead on Day 9, and one Group 2 male and one Group 4 female were both sacrificed in extremis on Day 8. These deaths were not attributed to treatment.

A higher incidence of depression, thinness, and anorexia was noted in the Group 3 animals. Erythema noted frequently during the treatment phase of the study ranged from severe to slight in Groups 2 and 4;

while erythema ranged from moderate to slight in Group 3. Edema, noted most frequently during the treatment phase, was generally observed as slight in all treated groups. Other dermal effects were noted frequently in all treated groups and included: blanching, eschar formation, epidermal scaling, fissuring, fissuring with bleeding, necrosis, raw areas, sloughing, and thickening.

Mean body weights were significantly lower in Groups 3 and 4 males, and Groups 2, 3, and 4 females by the end of the treatment phase. At termination, the Group 3 male weight was still significantly lower while all treated female groups were lower than control but not significant.

No treatment-related gross visceral lesions were noted. Microscopic evaluation did not reveal evidence of compound-related histomorphologic alteration. A variety of spontaneous disease lesions were observed in rabbits of all groups and lesions consistent with trauma were observed in the spinal cord of a Group 4 rabbit.

In conclusion, treatment-related effects on body weight, clinical observations, and dermal observations were noted, with the response being somewhat more severe in the Group 3 (corn oil vehicle) animals.

INTRODUCTION

The purpose of this study was to evaluate the systemic and local effects of repeated dermal contact of C-178 in rabbits. The study was initiated on February 9, 1981, and was terminated on March 11, 1981 (terminal necropsy dates - March 10 and 11, 1981).

VEHICLES AND TEST MATERIAL

Dukes® Corn Oil, (C. F. Sauer Company, Richmond, Virginia), a yellow liquid, and Acetone (Burdick and Jackson Labs, Inc., Muskegon, Michigan), a clear colorless liquid, were used as vehicles and were stored at room temperature. The test material, C-178, a clear colorless liquid, was received from the sponsor on February 5, 1981, and was stored under refrigeration. A purity of 100% was assumed for purposes of dosage calculations. Information on the synthesis, stability, as well as data on composition or other characteristics which define the test material, are on file with the sponsor.

TEST ANIMALS

Forty (twenty/sex) young adult New Zealand White rabbits were used in this study. The rabbits were selected from a larger pool of rabbits received from Dutchland Laboratory Animals, Inc., Denver, Pennsylvania, on January 5, 1981. Prior to initiation of the study, the rabbits were acclimated to laboratory conditions for five weeks. Ten days

prior to initiation of the study, the animals were examined for health status by a staff veterinarian. Two animals (one male and one female) were found clinically unacceptable and were replaced from the original pool of animals. After the health status examination, plexiglass neck collars were placed on each animal. The rabbits were uniquely identified by ear tags and housed individually in elevated metal cages. Commercial rabbit ration (Purina Lab Rabbit Chow[®]) and water (via automated watering system) were available ad libitum throughout the study. During the observation period, room temperature ranged from 64^o to 78^oF and humidity ranged from 32% to 60%. Body weights at initiation ranged from 2720 to 3650 grams for the males and from 2730 to 3455 grams for the females. Rabbits were used in this study because they have been used in safety evaluation studies and are required by the appropriate regulatory agencies.

METHODS

Groups and Dosage Levels

The rabbits were assigned to the following groups using a computerized randomization process. This process involved generating random numbers, assigning the numbers to the animals, ranking the random numbers, and assigning the animals to the groups.

<u>Group</u>	<u>Number of Animals</u>		<u>Dose Level</u>
	Males	Females	
1	5	5	Control
2	5	5	500 mg/kg of undiluted C-178
3	5	5	500 mg/kg of C-178 in corn oil
4	5	5	500 mg/kg of C-178 in acetone

Compound Preparation and Administration

Prior to initiation of this study, the dorsal area of each rabbit was clipped free of hair (approximately 10% of the total body surface). The area of exposure of three males and two females in each group was abraded prior to the first, third, sixth, and eighth doses. The abrasions were minor skin incisions which penetrated the stratum corneum, but were not sufficiently deep to disturb the dermis or to produce bleeding. The exposure area of the remaining two males and three females in each group was left intact.

Treated animals received the appropriate volume of test material applied by gentle inunction with a glass rod over the clipped area of abraded and unabraded skin for ten consecutive days.^a Group 2 was dosed with undiluted compound in which the dose factor was determined by obtaining the specific gravity (at room temperature). Group 3 was prepared with a 25% w/w solution of the compound in corn oil. The resulting solution was dosed volumetrically by determining the specific gravity (at room temperature) and dividing it into the dose factor which was predetermined by the known level and concentration. Group 4 was prepared with a 25% w/w solution of the compound in acetone and was dosed volumetrically by the same procedure as explained for Group 3. The Group 4 solution was separated into daily aliquots and sealed to keep the acetone vehicle from

^a Animals were not treated after the ten-day treatment period; however, animals were observed through termination of the study (nineteen to twenty days posttreatment).

evaporating. All test solutions were stored in amber colored bottles to protect the compound from light. The test material was administered dermally because potential human exposure is by the dermal route.

Observations and Records

All rabbits were observed twice daily for mortality and moribundity, and once daily for gross signs of dermal irritation and systemic toxicity. Dermal responses were scored according to the scoring system presented in the Key to Appendix 2. Scoring was performed prior to the first dose and daily thereafter. Body weights were recorded at initiation; on Days 3, 6, and 10; and then weekly until termination.

Sacrifice and Gross Pathology

At termination (Day 29 or 30)^a all remaining rabbits were sacrificed by exsanguination under sodium pentobarbital anesthesia (V-Pento, A. J. Buck and Son, Cockeysville, Maryland), necropsied, and gross observations recorded.

Tissue Preservation

The following tissues from each rabbit were preserved in 10% neutral buffered formalin: adrenals, brain (two sections), eyes, gonads, heart, intestine (duodenum, ileum, colon) kidneys, liver (right and left lobe), lung (right), mammary gland, mesenteric lymph node, pancreas, pituitary, prostate, salivary gland, sciatic nerve, skeletal muscle, skin

^a Due to scheduling, animals were not all sacrificed on the same day.

(treated and untreated), spinal cord (entire), spleen, stomach, thyroid, urinary bladder, uterus, and any unusual lesions.

Histopathology

The following tissues were embedded in Paraplast[®], sectioned, stained with hematoxylin and eosin, and evaluated histopathologically: brain, heart, kidneys, liver, lung, sciatic nerve, and two sections of the spinal cord taken from the lower lumbar region including one longitudinal and one transverse section.

Statistical Analysis

Statistical evaluation of body weights was performed by one-way analysis of variance (ANOVA) and covariance (ANCOVA) (Winer, 1971) with the initial (Day 0) body weights as covariates. The methods include Bartlett's test (Bartlett, 1937) for homogeneity of variances and a series of F-tests for determining the appropriateness of ANCOVA. Games and Howell's modification of Tukey's Studentized Range test (Games and Howell, 1976) was performed for comparison of both the unadjusted (ANOVA) and adjusted (ANCOVA) treatment means in the case of overall statistical significance. All significant testing was performed at the 5.0% (one-tailed) probability level.

The intervals analyzed were: Days 0-10 and Days 0-Termination. The first interval indicating the pretreatment (Day 0) and treatment phase (Days 1-10), and the second interval (Days 0-Termination) indicating the net body weight change during the study.



- 8 -

Statistically significant differences are designated as follows:

S- = Significantly lower than the control value.

Specimens, Raw Data, and Final Report Storage

All specimens, raw data, and the final report are stored in the archives of Hazleton Laboratories America, Inc.

RESULTS

Mortality

One Group 4 female was found dead on Day 9, and one Group 2 male and one Group 4 female were sacrificed in extremis on Day 8. The latter two rabbits were sacrificed due to an inability to use their hindlegs, apparently the result of injury and not treatment.

Clinical Observations

Individual daily clinical observations are presented in Appendix 1.

No unusual clinical observations were noted in the control animals during the study. Groups 2 and 4 exhibited sporadic instances of thinness and anorexia, while Group 3 exhibited more severe and consistent clinical effects including depression, thinness, anorexia, localized alopecia, and localized sores.

Dermal Irritation

Individual erythema and edema scores as well as other dermal effects are presented in Appendices 2A, 2B, and 2C, respectively.

No erythema was noted in any of the control animals throughout the study. Erythema ranging from severe to slight was noted frequently in Groups 2 and 4; while erythema ranging from moderate to slight was noted frequently in Group 3. Erythema observations were noted most frequently during the treatment phase and all erythema (except in one animal) was noted to clear by termination of the study.

Table 1
 Mean Body Weights and Mean Body Weight Changes (Grams)
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits

Group and Dose Level	Body Weights							Weight Change		
	Day 0	Day 3	Day 6	Day 10	Day 17	Day 24	Termination	Day 0- Day 10	Day 10- Termination	
Males										
1 0 mg/kg	Mean	2921.0	3063.0	3122.0	3188.0	3296.0	3390.0	3346.0	+267.0	+158.0
	S.D.	116.00	149.91	140.34	147.59	173.00	187.48	203.42	64.19	75.38
2 500 mg/kg	Mean	3188.0	3329.0	3248.0	3268.8	3372.5	3607.5	3521.3	+10.0	+252.5
	S.D.	228.08	232.79	229.42	194.92	213.13	237.96	214.80	55.98	115.07
3 500 mg/kg/ corn oil	Mean	3194.0	3181.0	2993.0	2705.0 ^{S-}	2944.0	3120.0	3022.0 ^{S-}	-489.0	+317.0
	S.D.	256.26	265.01	306.46	272.65	226.56	307.16	319.68	404.81	276.15
4 500 mg/kg/ acetone	Mean	3258.0	3213.0	3208.0	3128.0 ^{S-}	3272.0	3534.0	3484.0	-130.0	+356.0
	S.D.	283.61	219.48	214.32	215.02	208.25	259.87	254.08	140.22	56.94
Females										
1 0 mg/kg	Mean	3218.0	3449.0	3474.0	3567.0	3690.0	3806.0	3764.0	+349.0	+197.0
	S.D.	255.16	314.67	240.17	223.74	222.60	198.07	228.13	98.96	76.53
2 500 mg/kg	Mean	3085.0	3119.0	3090.0	3049.0 ^{S-}	3124.0	3348.0	3351.0	-36.0	+302.0
	S.D.	253.55	240.14	259.40	236.34	207.07	207.17	243.86	165.17	92.64
3 500 mg/kg/ corn oil	Mean	2979.0	3083.0	2928.0	2851.0 ^{S-}	3000.0	3244.0	3166.0	-128.0	+315.0
	S.D.	203.21	298.86	236.02	237.37	322.10	365.83	357.31	147.33	205.76
4 500 mg/kg/ acetone	Mean	2933.0	2972.0	2870.0	2866.7 ^{S-}	2970.0	3210.0	3148.3	-61.7	+201.7
	S.D.	168.99	240.59	247.39	250.42	310.00	316.07	350.01	38.80	136.00

No edema was noted in any of the control animals throughout the study. Edema, noted most frequently during the treatment phase, was observed as slight in all treated groups except for one Group 2 female which was noted as having moderate edema on Days 5 and 6.

Other dermal effects were not noted in any of the control animals throughout the study. Other dermal effects were noted frequently in all treated groups and were first observed during the treatment phase of the study. These effects included: blanching, eschar formation, epidermal scaling, fissuring, fissuring with bleeding, necrosis, raw areas, sloughing, and thickening. Several of these effects were noted through termination of the study in many animals.

Body Weights

Individual body weights, body weight changes, and mean body weights and body weight changes are presented in Appendix 3. Mean body weights and changes are presented in Table 1.

Mean body weights at initiation were essentially comparable for all groups. On Day 10, mean body weights were significantly lower in Groups 3 and 4 males as well as Groups 2, 3, and 4 females. By termination, Group 3 males were still significantly lower than control while all treated female groups were lower (not significantly) than control.

Gross Pathology

A summary of gross pathology findings is presented in Table 2.

No treatment-related gross visceral lesions were noted; however, skin lesions noted at gross necropsy were only present in treated groups as previously discussed.

Histopathology

Individual histopathology findings are presented in Table 3.

Microscopic evaluation revealed no compound-related histomorphologic alterations in the tissues examined. A variety of spontaneous disease lesions and incidental findings were noted as follows: lesions of encephalitozoonosis were present involving the central nervous system as well as visceral tissues. These lesions were composed of nonsuppurative encephalitis/meningoencephalitis, nonsuppurative myelitis, focal pneumonitis, nonsuppurative myocarditis, and slight or moderate focal nephropathy. A variety of other lesions were observed consisting of peribronchial and perivascular lymphoid hyperplasia in lung sections and medial calcification of the aorta in single Group 3 and Group 4 rabbits. Nonsuppurative pericholangitis and bile duct proliferation were noted in rabbits of all groups and focal hepatic necrosis was noted as a spontaneous disease lesion in Group 2 male rabbit No. E26629 and Group 4 female rabbit No. E26687. Kidney sections from nearly all rabbits revealed a variable degree of focal nephropathy with occasional foci of mineralization in the outer cortex. Sections of sciatic nerve from all rabbits were within

normal histologic limits. The spinal cord section from Group 4 female No. E26684 revealed hemorrhage, malacia, increased capillary formation, and glial cell response apparently resulting from severe trauma to the spinal cord.

In conclusion, microscopic evaluation of sections of brain, spinal cord, sciatic nerve, lung, heart, liver, and kidneys from rabbits which received the test material (C-178) undiluted, in corn oil, and in acetone via dermal application failed to reveal evidence of compound-related histomorphologic alteration. A variety of spontaneous disease lesions were observed in rabbits of all groups and lesions consistent with trauma were observed in the spinal cord of a Group 4 rabbit.

Table 2
 Summary of Gross Pathology Findings^a
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits

ORGAN AND DESCRIPTION	Group:		Males		Females	
	1	2	3	4	3	4
Dose Level (mg/kg):	0	500	500	500	500	500
			(corn oil)	(acetone)	(corn oil)	(acetone)
Number of rabbits examined	5	4(1)	5	5	5	5
Number with no gross visceral lesions	5	4	4	3	5	3(2)
					5	3(1)
SALIVARY GLANDS						
One dark red			1			
THYROID						
Pale			(1)			
LUNGS						
One lobe firm, dark red, and would not inflate upon perfusion			(1)			
All lobes bright red with dark red areas						(1)
GALLBLADDER						
Not evident at time of necropsy				1		
SPLEEN						
Pale area with dark red foci						(1)
KIDNEYS						
Pale cortex						(1)
ADRENALS						
Slightly enlarged				1		

^a Numbers indicate the incidence of the finding. Numbers in parentheses indicate that the animal exhibiting the finding was found dead or sacrificed in extremis during the study.

Table 2 - Continued
 Summary of Gross Pathology Findings^a
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits

ORGAN AND DESCRIPTION	Group:		Males		Females	
	1	2	3	4	3	4
Dose Level (mg/kg):	0	500	500	500	500	500
			(corn oil)	(acetone)	(corn oil)	(acetone)
STOMACH						
Contained clear, greenish fluid and dark brown material; cardiac portion contained dark brownish-red material and white mucus-like material						
Thickened walls						(1) (1)
INTESTINES						
Colon distended with firm fecal-like material						
Prominent Peyer's patches						(1) (1)
URINARY BLADDER						
Distended; tan to dark red, firm area on mucosal lining near neck						(1)
TESTES						
Soft						(1)

^a Numbers indicate the incidence of the finding. Numbers in parentheses indicate that the animal exhibiting the finding was found dead or sacrificed in extremis during the study.

Table 2 - Continued
 Summary of Gross Pathology Findings^a
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits

Dose Level (mg/kg)	Males		Females	
	1	2	3	4
0	0	500	0	500
		(corn oil)		(acetone)
				(corn oil)
				500
				4
				3
				2
				1
				0
				1

EXTERNAL OBSERVATIONS	Males		Females	
	1	2	3	4
PENIS				
Dark red and protruding	(1)			
FEET				
Crusty areas on hindpaws	1			
SKIN (TREATED)				
Thickened	2	1	3	1(1)
Epidermal scaling	3	4	5	3
Necrosis			1	(1)
Sloughing			2	
Raw areas			1	
Red			3	(1)
Edematous				(1)

^a Numbers indicate the incidence of the finding. Numbers in parentheses indicate that the animal exhibiting the finding was found dead or sacrificed in extremis during the study.

Key to Table 3

Type of Finding

- 0 = Tissue Absent
- X = Tissue Examined and Not Remarkable
- A = Autolysis
- P = Finding Present

Grading or Degree of Finding

- 1 = Minimal
- 2 = Slight
- 3 = Moderate
- 4 = Moderately Severe
- 5 = Severe

Table 3 - Continued
 Individual Histopathology Findings
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits

ORGAN AND DESCRIPTION	Group 1 - 0 mg/kg						Group 2 - 500 mg/kg									
	Males			Females			Males			Females						
	E	E	E	E	E	E	E	E	E	E	E	E				
KIDNEYS	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
Focal nephropathy	6	6	6	6	6	6	6	6	6	6	6	6	6	6		
Foci of mineralization	6	6	6	6	6	6	6	6	6	6	6	6	6	6		
SCIATIC NERVE	2	2	2	2	2	2	2	2	2	2	2	2	2	2		
	1	2	3	5	7	7	8	9	0	1	2	3	4	5	6	7
	1	2	3	1	1	1	1	1	3	2	1	1	2	3	1	1
	P								P			P				P
	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Animal Number:

Table 3 - Continued
 Individual Histopathology Findings
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits

ORGAN AND DESCRIPTION	Group 3 - 500 (mg/kg (corn oil))						Group 4 - 500 mg/kg (acetone)					
	Males			Females			Males			Females		
	E	E	E	E	E	E	E	E	E	E	E	E
HEART	X	X	X	X	X	X	X	X	X	X	X	X
Nonsuppurative myocarditis												
Medial calcification (aorta)												
LIVER												
Vacuolation of hepatocytes (centrilobular)												
Congestion												
Nonsuppurative pericholangitis												
Bile duct proliferation												
Hepatic necrosis (focal)												
KIDNEYS												
Focal nephropathy												
Foci of mineralization												
Congestion												
SCIATIC NERVE												

Animal
 Number:

Key to Appendix 1

A = Abraded
I = Intact
N = Appeared Normal
C = Collar in Mouth
D = Depressed
H = Hindleg Injury
L = Slightly Depressed
P = Localized Alopecia
S = Localized Sores
T = Thin
X = Anorexia

Explanation of Footnotes

- a Animal was unable to use it's hindlegs.
- b Localized sores and alopecia on these animals refer to the hind paws and/or legs.
- c The restraining collar was apparently dislocated and resulted in some bleeding from the animals mouth.

Key to Appendices 2A, 2B, and 2C

Evaluation of Skin Reactions

Erythema

- 0 = None
- 1 = Slight (barely perceptible)
- 2 = Moderate (well defined)
- 3 = Severe (beet red)

Edema

- 0 = None
- 1 = Slight (barely perceptible to well defined by definite raising)
- 2 = Moderate (raised approximately 1 mm)
- 3 = Severe (raised more than 1mm)

Other Dermal Effects

- B = Blanching
- ✓ C = Eschar
- ✓ E = Epidermal Scaling
- F = Fissuring
- L = Fissuring with Bleeding
- ✓ N = Necrosis
- R = Raw Areas
- ✓ S = Sloughing
- T = Thickening

Explanation of Footnote

^a Animal sacrificed in extremis on Day 8 after observations were made.

Appendix 2A - Continued
 Individual Daily Evaluation of Skin Reactions
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits
 Erythema Scores

Females

Animal Number	Site	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30							
Group 1 - 0 mg/kg																																							
E26667	A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0		
E26668	A	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
E26669	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
E26670	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
E26672	I	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Group 2 - 500 mg/kg																																							
E26673	A	0	0	1	3	3	3	3	3	3	3	3	3	3	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	
E26674	A	0	0	2	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
E26675	I	0	0	2	3	3	3	3	3	3	3	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
E26676	I	0	0	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
E26677	I	0	0	1	3	3	3	3	3	3	3	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Group 3 - 500 mg/kg (corn oil)																																							
E26679	A	0	0	1	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
E26680	A	0	0	1	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
E26681	I	0	0	1	2	2	2	2	2	2	2	2	2	2	2	2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
E26682	I	0	0	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
E26683	I	0	0	1	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Group 4 - 500 mg/kg (acetone)																																							
E26684	A	0	0	1	2	3	3	3	3	3	3 ^a																												
E26685	A	0	0	1	1	2	2	2	2	2	2																												
E26687	I	0	0	1	2	3	3	3	3	3	3																												
E26688	I	0	0	1	1	3	3	3	3	3	3																												
E26689	I	0	0	1	1	2	2	2	2	2	2																												

Found Dead

Appendix 2C
 Individual Daily Evaluation of Skin Reactions
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits
 Other Dermal Effects

Males

Animal Number	Site	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Group 1 - 0 mg/kg																
E26621	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26622	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26623	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26625	I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26627	I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 2 - 500 mg/kg																
E26628	A	-	-	-	-	-	-	-	Y	NT	NT	DNT	BNT	BEFHT	BEFHT	EFHT
E26629	A	-	-	-	-	-	-	-	-	N ^a	N	NT	NT	ENT	ENT	ENT
E26630	A	-	-	-	-	-	-	-	N	N	N	BNT	FNT	EFNT	EFNT	EFNT
E26631	I	-	-	-	-	-	-	-	N	N	T	T	T	EFHT	EFHT	EFHT
E26632	I	-	-	-	-	-	-	-	Y	Y	Y	Y	Y	Y	Y	Y
	%N	0	0	0	0	0	0	0	40	75	75	75	75	100	100	100
Group 3 - 500 mg/kg (corn oil)																
E26633	A	-	-	-	-	-	-	-	-	B	B	B	BT	FNT	FNT	EFNT
E26634	A	-	-	-	-	-	-	-	-	-	Y	Y	FT	FHRST	LNRST	EFNST
E26635	A	-	-	-	-	-	-	-	-	-	-	B	B	BC	BC	CE
E26636	I	-	-	-	-	-	-	-	-	T	T	T	FT	FST	FST	FST
E26637	I	-	-	-	-	-	-	-	-	-	T	T	T	CT	CST	CST
	%N	0	0	0	0	0	0	0	0	0	0	0	0	0	40	40
Group 4 - 500 mg/kg (acetone)																
E26638	A	-	-	-	-	-	-	-	NT	NT	NT	NT	NT	EFNT	EFNT	EFNT
E26639	A	-	-	-	-	-	-	-	FN	FN	FN	FNT	FNT	EFNT	EFNT	EFNT
E26640	A	-	-	-	-	-	-	-	B	B	T	T	NT	BEFNT	BEFNT	EFNT
E26641	I	-	-	-	-	-	-	-	B	B	T	T	T	BET	BET	ET
E26643	I	-	-	-	-	-	-	-	-	BT	NT	NT	FNT	ELNST	ELNST	EFNST
	%N	0	0	0	0	0	20	40	60	60	60	80	80	80	80	80

Appendix 2C - Continued
 Individual Daily Evaluation of Skin Reactions
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits
 Other Dermal Effects

Males

Animal Number	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
	Group 1 - 0 mg/kg															
E26621	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26622	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26623	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26625	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26627	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	Group 2 - 500 mg/kg															
E26628	EFNST	ENST	ENST	ENS	ENS	ENRST	ENS	ENS	ENS							
E26629	ENST	EFNST	ENST	ENS	ENS	ENS	ENS	ENS	ENS	ENS	ENS	ENS	ENS	ENS	ENS	ENS
E26630	ENST	ENST	ENRST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENRST	ENRST	ENRST
E26631	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST
E26632	100	100	100	100	100	75	75	75	75	75	75	75	50	50	50	50
	Group 3 - 500 mg/kg (corn oil)															
E26633	ENST	ET	ET	EST	EST	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET
E26634	ENST	ES	ES	ES	ES	ES	EST	EST	EST							
E26635	CE	CE	CE	CE	CE	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET
E26636	FST	EFST	EST	EST	EST	EST	E	E	E	E	E	E	E	E	E	E
E26637	CST	ET	ET	EST	EST	EST	E	E	E	E	E	E	E	E	E	E
	Group 4 - 500 mg/kg (acetone)															
E26638	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST
E26639	EFNST	EFNST	EFNST	EFNST	EFNST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST
E26640	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST
E26641	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET	ET
E26643	EFNST	ENRST	ENRST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST	ENST
	80	80	80	80	80	40	40	40	40	40	40	40	20	20	20	20

Appendix 2C - Continued
 Individual Daily Evaluation of Skin Reactions
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits
 Other Dermal Effects

Females

Animal Number	Site	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14
Group 1 - 0 mg/kg																
E26667	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26668	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26670	I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26672	I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
E26673	I	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Group 2 - 500 mg/kg																
E26673	A	-	-	-	-	-	-	-	N	N	N	NT	NT	EFNT	EFNT	EFNT
E26674	A	-	-	-	-	-	-	-	NT	NT	NT	NT	NT	ENT	ENT	ENT
E26675	I	-	-	-	-	-	-	-	NT	NT	NT	NT	NT	BENT	BENT	BENT
E26676	I	-	-	-	-	-	-	-	T	T	T	T	FT	BFNT	BFNT	BFNT
E26677	I	-	-	-	-	-	-	-	N	N	NT	NT	NT	BEFNT	BEFNT	BEFNT
Group 3 - 500 mg/kg (corn oil)																
E26679	A	-	-	-	-	-	-	-	B	B	B	T	FT	CLST	CLST	CFST
E26680	A	-	-	-	-	-	B	B	B	B	BT	BT	BFT	BCELRT	BCELRT	CEFST
E26681	I	-	-	-	-	-	B	B	B	B	BT	BT	BT	BCELRT	BCELRT	CEFST
E26682	I	-	-	-	-	-	-	-	-	B	BT	BFT	FNT	ELNSRT	ELNSRT	ELNST
E26683	I	-	-	-	-	-	B	B	B	B	T	T	T	FHRT	FHRT	FNRST
Group 4 - 500 mg/kg (acetone)																
E26684	A	-	-	-	-	-	-	-	-	T ^a	Found Dead					
E26685	A	-	-	-	-	-	-	-	H	NT	NT	NT	NT	BENT	BENT	ENT
E26687	I	-	-	-	-	H	N	H	H	N	N	N	NT	ELMRT	ELMRT	EFNRT
E26688	I	-	-	-	-	-	-	-	-	T	NT	NT	FNT	ELMRT	ELMRT	EFNRT
E26689	I	-	-	-	-	-	B	B	B	B	FT	FT	FT	EFRT	EFRT	EFNT

Appendix 3
Individual and Mean Body Weights and Body Weight Changes (Grams)
Ten-Day Dermal Toxicity Study of C-178 in Rabbits

Males

Animal Number	Site	Body Weights					Day 24	Termination	Weight Change		
		Day 0	Day 3	Day 6	Day 10	Day 17			Day 0- Day 10	Day 10- Termination	Initiation- Termination
E26621	A	2990	3180	3225	3315	3470	3550	3560	+325	+245	+570
E26622	A	2720	2810	2895	2940	3020	3080	3050	+220	+110	+330
E26623	A	3005	3065	3095	3185	3280	3370	3240	+180	+ 55	+235
E26625	I	2930	3090	3150	3220	3300	3430	3400	+290	+180	+470
E26627	I	2960	3170	3245	3280	3410	3520	3480	+320	+200	+520
Mean		2921.0	3063.0	3122.0	3188.0	3296.0	3390.0	3316.0	+267.0	+158.0	+425.0
S.D.		116.00	149.90	140.34	147.59	173.00	187.48	203.42	64.19	75.38	130.92
E26628	A	3395	3460	3325	3335	3440	3680	3650	- 60	+315	+255
E26629	A	2905	2950	2880	2565 ^a	--	--	--	--	--	--
E26630	A	3025	3325	3195	3015	3100	3290	3200	- 10	+185	+175
E26631	I	3185	3345	3360	3245	3340	3600	3625	+ 60	+380	+440
E26632	I	3430	3565	3480	3480	3610	3860	3610	+ 50	+130	+180
Mean		3188.0	3329.0	3248.0	3268.8	3372.5	3607.5	3521.3	+ 10.0	+252.5	+262.5
S.D.		228.08	232.79	229.42	194.91	213.13	237.96	214.80	55.98	115.07	123.86
E26633	A	3480	3510	3370	2930	3270	3570	3445	-550	+515	- 35
E26634	A	3005	2820	2515	2450	2740	2880	2675	-555	+225	-330
E26635	A	2860	3030	3010	3045	2820	3020	2945	+185	-100	+ 85
E26636	I	3260	3310	3060	2645	3090	3290	3250	-615	+605	- 10
E26637	I	3365	3235	3010	2455	2800	2840	2795	-910	+340	-570
Mean		3194.0	3181.0	2993.0	2705.0 ^{S-}	2944.0	3120.0	3022.0 ^{S-}	-489.0	+317.0	-172.0
S.D.		256.26	265.01	306.46	272.65	226.56	307.16	319.68	404.81	276.15	271.31
E26638	A	3170	3330	3225	3015	3160	3390	3375	-155	+360	+205
E26639	A	3650	3435	3500	3390	3550	3780	3805	-260	+415	+155
E26640	A	2875	2860	2895	2845	3000	3170	3125	- 30	+280	+250
E26641	I	3225	3270	3200	3280	3370	3770	3600	+ 55	+320	+375
E26643	I	3370	3170	3220	3110	3280	3560	3515	-260	+405	+145
Mean		3258.0	3213.0	3208.0	3128.0 ^{S-}	3272.0	3534.0	3484.0	-130.0	+356.0	+226.0
S.D.		203.61	219.48	214.32	215.02	208.25	259.87	254.08	140.22	56.94	93.30

^a Terminal weight when animal was sacrificed in extremis on Day 8; value excluded from mean calculations.
NOTE: A = Abraded; I = Intact

Appendix 3 - Continued
 Individual and Mean Body Weights and Body Weight Changes (Grams)
 Ten-Day Dermal Toxicity Study of C-178 in Rabbits

Females

Animal Number	Site	Body Weights					Weight Change			
		Day 0	Day 3	Day 6	Day 10	Day 17	Day 24	Day 0- Day 10	Day 10- Termination	Initiation- Termination
Group 1 - 0 mg/kg										
E26667	A	3180	3420	3510	3670	3800	3950	4490	+150	+640
E26668	A	3170	3425	3420	3545	3590	3750	+375	+90	+465
E26669	I	3450	3745	3740	3755	3910	3760	+305	+275	+580
E26670	I	2835	2955	3100	3190	3350	3530	+355	+255	+610
E26672	I	3455	3700	3600	3675	3800	4040	+220	+215	+435
Mean		3218.0	3449.0	3474.0	3567.0	3690.0	3806.0	+349.0	+197.0	+546.0
S.D.		255.16	314.67	240.17	223.74	222.60	198.07	98.96	76.53	90.79
Group 2 - 500 mg/kg										
E26673	A	3065	3290	3345	3280	3240	3540	+215	+235	+450
E26674	A	3070	3125	2890	2960	3160	3380	-110	+420	+310
E26675	I	3445	3350	3330	3210	3200	3360	-235	+230	-5
E26676	I	3115	3095	3120	3110	3260	3460	-5	+385	+380
E26677	I	2730	2735	2765	2695	2760	3000	-45	+240	+195
Mean		3085.0	3119.0	3090.0	3049.0 ^a	3624.0	3348.0	-36.0	+302.0	+266.0
S.D.		253.55	240.14	259.40	236.34	207.07	207.17	165.17	92.64	178.37
Group 3 - 500 mg/kg (corn oil)										
E26679	A	2895	3130	3010	3000	3140	3350	+105	+325	+430
E26680	A	3235	3370	3170	3095	3270	3500	-140	+295	+155
E26681	I	3150	3345	3070	2915	3230	3640	-235	+630	+395
E26682	I	2760	2670	2575	2490	2500	2780	-270	+270	0
E26683	I	2855	2900	2815	2755	2860	2950	-100	+55	-45
Mean		2979.0	3083.0	2928.0	2851.0 ^a	3000.0	3244.0	-128.0	+315.0	+187.0
S.D.		203.21	298.86	236.02	237.37	322.10	365.83	147.33	205.76	219.16
Group 4 - 500 mg/kg (acetone)										
E26684	A	2845	2950	2770	2762 ^a	--	--	--	--	--
E26685	A	3035	3190	2770	2250	Found Dead	--	--	--	--
E26687	I	3180	3240	3290	3150	3320	3510	-30	+350	+320
E26688	I	2825	2785	2870	2775	2860	3240	-50	+370	+370
E26689	I	2780	2695	2650	2675	2730	2880	-105	+125	+20
Mean		2933.0	2972.0	2870.0	2866.7 ^a	2970.0	3210.0	-61.7	+281.7	+220.0
S.D.		168.99	240.59	247.39	250.42	310.00	316.07	38.80	136.00	173.21

^a Terminal weight when animal was sacrificed in extremis on Day 8; value excluded from mean calculations.
 NOTE: A = Abraded; I = Intact

Appendix 4
References
Ten-Day Dermal Toxicity Study of C-178 in Rabbits

STATISTICAL METHODS

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APR 18 1995

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Sincerely,

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

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CECATS DATA: Submission # BEHQ. 0992-12452 SEQ. A

TYPE: INT SUPP FLWP

SUBMITTER NAME: Rhone-Poulenc Inc.

INFORMATION REQUESTED: FLWP DATE

- 0501 NO INFO REQUESTED
- 0502 INFO REQUESTED (TECH)
- 0503 INFO REQUESTED (VOL ACTIONS)
- 0504 INFO REQUESTED (REPORTING RATIONAL.F.)

DISPOSITION:

- 0678 REFER TO CHEMICAL SCREENING
- 0678 CAP NOTICE

0678 VOLUNTARY ACTIONS:

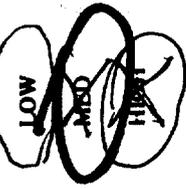
- 0401 NO ACTION REPORTED
- 0402 STUDIES PLANNED/IN PROGRESS
- 0403 NOTIFICATION OF WORKING CONDITIONS
- 0404 LABEL/MSDS CHANGES
- 0405 PROCESS/HANDLING CHANGES
- 0406 APP/USE DISCONTINUED
- 0407 PRODUCTION DISCONTINUED
- 0408 CONFIDENTIAL

SUB. DATE: 09/04/92 OTS DATE: 09/22/92 CSRAD DATE: 02/16/95

CHEMICAL NAME: _____ CASE# 42978-66-5

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	ECO/AQUA TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	ENV. OCCUR/REL/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 REQUEST 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	0299 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		

TRIAS DATA: NON-CBI INVENTORY YES NO IN PENDING PRODUCTION:



SPECIES: ROT TOXICOLOGICAL CONCERN: LOW

ONGOING REVIEW: YES (DROPP/REFER) NO (CONTINUE) REFTR

CAS SR

10595212

8 (E) -12452A

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SUBACUTE DERMAL TOXICITY IN RABBITS IS OF LOW CONCERN. DOSAGE IN EACH OF THREE GROUPS WAS 500 MG/KG/DAY. MORTALITY DATA ARE AS FOLLOWS: NEAT TEST SUBSTANCE (0/5 M, 0/5 F), SUBSTANCE IN CORN OIL (0/5 M, 1/5 F), AND SUBSTANCE IN ACETONE (0/5 M, 1/5 F). ONE MALE GIVEN NEAT TEST SUBSTANCE AND ONE FEMALE GIVEN TEST SUBSTANCE IN ACETONE WERE SACRIFICED ON DAY 8 DUE TO AN INABILITY TO USE THEIR HIND LEGS FROM THE RESULT OF INJURY AND NOT TREATMENT. DERMAL REACTIONS INCLUDED SLIGHT TO SEVERE ERYTHEMA FOR THE NEAT SUBSTANCE AND THE SUBSTANCE IN ACETONE, AND SLIGHT TO MODERATE FOR THE SUBSTANCE IN CORN OIL. EDEMA WAS SLIGHT IN ALL TREATED ANIMALS EXCEPT FOR MODERATE EDEMA IN ONE FEMALE THAT RECEIVED THE NEAT TEST SUBSTANCE. OTHER DERMAL EFFECTS NOTED FREQUENTLY IN ALL TREATED GROUPS INCLUDED BLANCHING, ESCHAR FORMATION, EPIDERMAL SCALING, FISSURING WITH BLEEDING, NECROSIS, RAW AREAS, SLOUGHING, AND THICKENING. AT THE END OF THE TREATMENT PERIOD, MEAN BODY WEIGHTS WERE SIGNIFICANTLY DECREASED IN FEMALES OF ALL THREE GROUPS AND MALES GIVEN THE TEST SUBSTANCE IN CORN OIL OR ACETONE. BESIDES SKIN LESIONS, THERE WERE NO TREATMENT-RELATED GROSS PATHOLOGY OR HISTOLOGIC FINDINGS.