1-25-94

FINAL

DATA EVALUATION REPORT

Rejex-it AP-50

Study Type: Acute Oral Toxicity in Rats

Prepared for:

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031

January 1994

Principal Reviewer	Kate Rantz Kate Rantz, M.P.H.	Date 1/13/94
Independent Reviewer	Carrie Rabe Carrie Rabe, Ph.D.	Date 1/24/94
QA Reviewer	William L McLellan William McLellan, Ph.D.	Date 1/25/94

Contract Number: 68D10075
Work Assignment Number: 3-36
Clement Number: 154
Project Officer: Caroline Gordon

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EPA Reviewer: J. Thomas McClintock
Biological Section, Science Analysis Branch
Health Effects Division

Signature: J. Thomas McClintock
Date: 2/9/94

EPA Section Head: Roy Sjoblad
Biological Section, Science Analysis Branch
Health Effects Division

Signature: R D. Sjoblad
Date: 4/15/94

DATA EVALUATION REPORT

STUDY TYPE:	Guideline series 81-1; acute oral toxicity in rats
CAS NUMBER:	
TOX CHEM NUMBER:	
MRID NUMBER:	426087-02
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it AP-50
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305696
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Acute Oral Toxicity Study of Rejex-it AP-50 in Rats
AUTHOR:	Steven M. Glaza
STUDY COMPLETED:	July 7, 1992
QUALITY ASSURANCE:	The test was performed under Good Laboratory Practice Standards. A Quality Assurance Statement, signed July 7, 1992, was submitted.
CONCLUSIONS:	Estimated acute oral LD_{50} for males: >5000 mg/kg body weight Estimated acute oral LD_{50} for females: >5000 mg/kg body weight
CORE CLASSIFICATION:	Core Supplementary. This study satisfies the guideline requirements (81-1) for an acute oral toxicity study in rodents. However, insufficient

data were reported about the test material, i.e., lot number, stability, and purity were not provided. This study may be upgraded pending submission of these data.

TOXICITY CATEGORY: IV (Caution)

A. MATERIALS

Test Compound

Test material:	Rejex-it AP-50
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	White powder
Storage condition:	Room temperature
Stability:	Determined by sponsor
Vehicle:	Corn oil
Concentration in vehicle:	0.25 g/mL
Dose level:	5000 mg/kg body weight
Dose volume:	20 mL/kg body weight (4.7-5.8 mL, males; 4.3-4.6 mL, females)

Note: The guidelines (81-1) recommend that the dose volume should not exceed 10 mL/kg for non-aqueous solutions.

Controls

There were no controls.

Test Animals

Species:	Albino rat
Strain:	Crl:CD®BR
Source:	Charles River Laboratories, Inc., Portage, MI
Sex:	5 males and 5 females
Age:	Young adult
Initial body weights (fasted):	214-230 g for males; 234-290 g for females
No. animals:	5/sex/dose
Temperature:	22-27°C
Relative humidity:	39-54%
Photoperiod:	12-hour light/dark cycle
Feeding:	Purina Certified Rodent Chow #5001, *ad libitum*
Water:	*Ad libitum*
Acclimation period:	At least 7 days
Housing:	5/cage; sexes separate
Identification:	Ear tags
Selection:	Healthy animals within unspecified weight limits were selected

B. TEST PERFORMANCE

Method of administration:	Oral gavage
Animals fasted:	food was withheld 17-20 hours before dosing
Dosing:	Once __x__; Other _____ (describe)
Observation period:	14 days
Observation frequency:	Clinical observations and mortality checks were conducted 1, 2.5, and 4 hours after dosing. Clinical observations were econducted daily and mortality checks were made twice daily thereafter for 14 days.
Body weight interval:	Body weights were measured day 0 (before dosing), day 7, and day 14 (study termination).
Gross pathology:	Yes
Histopathology:	No

C. RESULTS

Mortality

There were no deaths during the study.

Clinical observations

Clinical signs of toxicity included yellow-stained urogenital areas in 3/5 males at days 1 and 2, and soft stool in 1/5 females 4 hours post-treatment.

Body weights

All rats gained weight by the end of the 14-day observation period.

Gross necropsy

No compound-related changes were observed in any rats.

LD_{50} determination

The estimated acute oral LD_{50} for male and female rats was >5000 mg/kg body weight.

D. REVIEWERS' COMMENTS

Under these study conditions, the estimated acute oral LD_{50} for both male and female rats administered Rejex-it AP-50 was greater than 5000 mg/kg body weight. Clinical signs of toxicity included yellow-stained urogenital areas (3 rats) and soft stool in 1 rat. These effects may have been due to the large volume of corn oil that was administered. This LD_{50} corresponds to Toxicity Category IV (Caution).

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The study was done at the limit dose (5 g/kg) specified in guideline series 81-1.

FINAL

DATA EVALUATION REPORT

Rejex-it AP-50

Study Type: Acute Dermal Toxicity in Rabbits

Prepared for:

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
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January 1994

Principal Reviewer	Kate Rantz, M.P.H.	Date 1/13/94
Independent Reviewer	Carrie Rabe, Ph.D.	Date 1/24/94
QA Reviewer	William McLellan, Ph.D.	Date 1/25/94

Contract Number: 68D10075
Work Assignment Number: 3-36
Clement Number: 155
Project Officer: Caroline Gordon

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Guideline Series 81-2: Acute Dermal Toxicity in Rabbits

EPA Reviewer: J. Thomas McClintock
Biological Section, Science Analysis Branch
Health Effects Division

Signature: J. Thomas McClintock
Date: 2/9/94

EPA Section Head: Roy Sjoblad
Biological Section, Science Analysis Branch
Health Effects Division

Signature: R D Sjoblad
Date: 4/15/94

DATA EVALUATION REPORT

STUDY TYPE:	Guideline series 81-2; acute dermal toxicity in rabbits
CAS NUMBER:	
TOX CHEM NUMBER:	
MRID NUMBER:	426087-03
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it AP-50
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305700
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Acute Dermal Toxicity Study of Rejex-it AP-50 in Rabbits
AUTHOR:	Steven M. Glaza
STUDY COMPLETED:	July 7, 1992
QUALITY ASSURANCE:	The test was performed under Good Laboratory Practice Standards. A Quality Assurance Statement. signed July 7, 1992, was submitted.
CONCLUSIONS:	Estimated acute dermal LD_{50} for males: >2000 mg/kg body weight Estimated acute dermal LD_{50} for females: >2000 mg/kg body weight
CORE CLASSIFICATION:	Core Guideline. This study satisfies the guideline requirements (81-2) for an acute dermal toxicity study in rabbits.

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TOXICITY CATEGORY: III (Caution)

A. MATERIALS

Test Compound

Test material:	Rejex-it AP-50
Lot no.:	56-612-69-02
Purity:	Determined by sponsor
Physical description:	White powder
Storage condition:	Room temperature
Stability:	Determined by sponsor
Vehicle:	The test material was moistened with an unspecified amount of 0.9% saline
Dose level:	2000 mg/kg body weight (limit dose)

Controls

None.

Test Animals

Species:	Albino rabbits
Strain:	Hra:(NZW)SPF
Source:	Hazleton Research Products, Inc., Kalamazoo, MI
Sex:	5 males and 5 females
Age:	Young adult
Initial body weights:	2114-2364 g for males; 2016-2262 g for females
No. animals:	5/sex/dose
Temperature:	20-25°C
Relative humidity:	36-65%
Photoperiod:	12-hour dark/12-hour light cycle
Feeding:	Purina High Fiber Rabbit Chow #5326, measured amount daily
Water:	*Ad libitum*
Acclimation period:	At least 7 days
Housing:	Individual
Identification:	Ear tags
Selection:	Healthy animals within unspecified weight limits were selected

B. TEST PERFORMANCE

Application

The hair on the back of each rabbit (approximately 10% of the total body surface area) was clipped on the day before dosing. The test material (2000 mg/kg body weight) was moistened with an unspecified amount of 0.9% saline and applied to the intact skin of each rabbit. The area of application was covered with a 10 cm X 10 cm gauze patch, secured with paper tape, and wrapped with Saran Wrap and Elastoplast tape. After 24 hours the wrappings were removed. Excess test material was washed from the test site with tap water and paper towels.

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Observation period

Observations for clinical signs of toxicity were made 1, 2.5, and 4 hours after application of the test material. During the 14-day observation period, clinical observations and mortality checks (morning and afternoon) were made daily. The initial observation for dermal response was approximately 30 minutes after removal of the test material at days 3, 7, 10, and 14, according to the Draize technique.

Body weight interval

Body weights were measured day 0 (before application) and on observation days 7 and 14.

Gross pathology: Yes
Histopathology: No

C. RESULTS

Clinical observations

No overt signs of toxicity were observed. Table 1 shows the incidence of dermal irritation observations.

Body weights

All rabbits had gained weight by the end of the study. Minor weight loss (1-3%) was observed in 2 males and 2 females between days 7 and 14.

Mortality

All treated animals (5 males and 5 females) dosed with 2000 mg/kg body weight survived until study termination.

Table 1. Incidence of Dermal Irritation Scores (Draize Technique)

	Observation Period (days)				
	1	3	7	10	14
			Males (n=5)		
Erythema	0	1	1	0	0
Edema	0	2	0	0	0
Atonia	4	0	0	0	0
Desquamation	0	0	2	1	0
Coriaceousness	0	0	0	0	0
Fissuring	0	0	0	0	0
			Females (n=5)		
Erythema	0	0	0	0	0
Edema	2	2	0	0	0
Atonia	5	0	0	0	0
Desquamation	0	0	1	0	0
Coriaceousness	0	0	0	0	0
Fissuring	0	0	0	0	0

Gross necropsy

No compound-related gross changes were observed in any rabbit.

LD_{50} determination

The estimated acute dermal LD_{50} for male and female rabbits was greater than 2000 mg/kg body weight (limit dose), which corresponds to Toxicity Category III (Caution).

D. REVIEWERS' COMMENTS

The estimated acute dermal LD_{50} for male and female rabbits exposed to Rejex-it AP-50 under these study conditions was >2000 mg/kg body weight, which corresponds to Toxicity Category III (Caution). The dose level used in this study met the limit dose designated in the guideline. This study satisfies the guideline requirements (81-2) for an acute dermal toxicity study in rabbits.

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FINAL

DATA EVALUATION REPORT

Rejex-it AP-50

Study Type: Primary Eye Irritation Study in Rabbits

Prepared for:

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
Arlington, VA 22202

Prepared by:

Clement International Corporation
9300 Lee Highway
Fairfax, VA 22031

January 1994

Principal Reviewer Kate Rantz Date 1/13/94
Kate Rantz, M.P.H.

Independent Reviewer Carrie Rabe Date 1/24/94
Carrie Rabe, Ph.D.

QA Reviewer William L McLellan Date 1/25/94
William McLellan, Ph.D.

Contract Number: 68D10075
Work Assignment Number: 3-36
Clement Number: 156
Project Officer: Caroline Gordon

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EPA Reviewer: J. Thomas McClintock
Biological Section, Science Analysis Branch
Health Effects Division

Signature: J Thomas McClintock
Date: 2/9/94

EPA Section Head: Roy Sjoblad
Biological Section, Science Analysis Branch
Health Effects Division

Signature: Roy D. Sjoblad
Date: 4/14/94

DATA EVALUATION REPORT

STUDY TYPE: Guideline series 81-4; primary eye irritation study in rabbits

CAS NUMBER:

TOX CHEM NUMBER:

MRID NUMBER: 426087-04

PC NUMBER: 128725

TEST MATERIAL: Rejex-it AP-50

SYNONYM(S): Methyl anthranilate (active ingredient)

SPONSOR: ERM Program Management Company
McLean, Virginia

STUDY NUMBER: HWI 20305708

TESTING FACILITY: Hazleton Wisconsin, Inc.
Madison, Wisconsin

TITLE OF REPORT: Primary Eye Irritation Study of Rejex-it AP-50 in Rabbits

AUTHOR: Steven M. Glaza

STUDY COMPLETED: June 18, 1992

QUALITY ASSURANCE: The test was performed under Good Laboratory Practice Standards. A Quality Assurance Statement signed June 18, 1992, was submitted.

CONCLUSIONS: Under the conditions of this study, Rejex-it AP-50 produced moderate to severe conjunctival irritation (Draize scores 2 and 3 at 24 hours) and corneal and iridal involvement (scattered or diffuse corneal opacity (Draize score 1 at 24 hours) and circumcorneal injection in iris) in rabbit eyes which cleared within 14 days of treatment. Based

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on these findings, the test material was classified Toxicity Category II.

CORE CLASSIFICATION: Core Supplementary. This study satisfies the guideline requirements (81-4) for a primary eye irritation study in rabbits. However, there were insufficient data describing the test material (i.e., purity, stability, and lot number were not reported). This study may be upgraded pending submission of these data.

TOXICITY CATEGORY: II (Warning)

A. MATERIALS

Test Compound

Test material:	Rejex-it AP-50
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	White powder
Storage condition:	Room temperature
Stability:	Determined by sponsor
Vehicle:	None
Bulk density:	0.39 g/mL
Dose volume:	0.1 mL (dose equivalent)
Dose level:	0.04 g

Test Animals

Species:	Albino rabbits
Strain:	Hra:(NZW)SPF
Source:	Hazleton Research Products, Inc., Kalamazoo MI
Sex:	3 males and 3 females
Age:	Adult
Body weight:	2100-2262 g, males; 2130-2302 g, females
No. animals:	3/sex/dose
Temperature:	20-25°C
Relative humidity:	36-65%
Photoperiod:	12-hour dark/12-hour light cycle
Feeding:	Purina High Fiber Rabbit Chow #5326, measured amount daily
Water:	*Ad libitum*
Selection:	Animals free of ocular injury or irritation
Acclimation period:	At least 7 days
Housing:	Individual
Identification:	Ear tag

B. TEST PERFORMANCE

Test Material Application

Eyes were examined the day before application using sodium fluorescein dye. The solid test material (0.04 g; 0.1 mL, dose equivalent) was placed in the everted lower lid of the right eye of each rabbit. The upper and lower lids were held together for 1 second and then released. The left eye of each animal served as the untreated control. The eyes of the rabbits were not flushed.

Observation Period

Observations for ocular irritation were made at 1, 24, 48, 72, and 96 hours, and days 7 and 14 after treatment.

Scoring System

Eyes were examined and scored for ocular lesions using the Draize scoring system. Sodium fluorescein was used to help assess corneal injury at all examinations except 1 hour after dosing.

C. RESULTS

Individual eye irritation scores and clinical observations are presented in Table 1. Blanching and purulent and/or clear discharge of the conjunctivae were seen at hours 1, 24, 48, and 72 and were clear at 96 hours. Corneal epithelial peeling were observed in most animals at 1 hour and was clear by day 7. Pannus was seen in 2/6 animals at day 7. By day 14, all clinical signs of eye irritation had cleared.

Table 1. Individual Eye Irritation Scores (Draize Technique)

Animal No.	Cornea		Iris	Conjunctivae		
	Opacity	Involvement	Irritation	Redness	Chemosis	Discharge
			1 hour			
1[t]	1[j]	2	1[i]	2[b]	3	2[d]
2[u]	1[j]	1	1[i]	2[b]	3	2[c]
3[u]	1	4	1[i]	2[b]	3	2[c]
4[u]	1[j]	1	1[i]	2[b,e**]	3	2[c]
5[u]	1[j]	4	1[i]	2[b]	2	2[d]
6[u]	1[j]	1	1[i]	2[b,e**]	3	2[d]
			24 hours			
1	1[j]	4	1[i]	2[b,e**]	2	1[d]
2	1[j]	2	1[i]	3[b]	2	2[d]
3	1[j]	4	1[i]	3[b]	2	2[d]
4	1[j]	1	1[i]	2[b, e,**]	1	1[c]
5	1[j]	3	1[i]	2[b]	2	1[d]
6	1[j]	2	1[i]	2[b]	1	1[c]

Table 1. Individual Eye Irritation Scores (continued)

Animal No.	Cornea		Iris	Conjunctivae		
	Opacity	Involvement	Irritation	Redness	Chemosis	Discharge
			48 hours			
1	1[j]	4	1[i]	2[b,e]	2	1[d]
2	1[j]	2	1[i]	2[b]	2	1[d]
3	1[j]	2	1[i]	2[b]	1	1[d]
4	1	1	0	2[e**]	0	0
5	1[j]	3	1[i]	2	0	0
6	1[j]	1	1[i]	2[e**]	1	0
			72 hours			
1	1[j]	1	0	2[e]	1	0
2	1	1	1[i]	2	1	1[c]
3	1[j]	1	0	2	1	2[c]
4	0	0	1[i]	2[a,e**]	1	1[c]
5	1[j]	1	1[i]	2	1	1
6	0	0	0	2[e**]	1	0
			96 hours			
1	1[j]	1	0	1	1	0
2	0	0	0	1	1	0
3	1[j]	1	0	2	1	0
4	0	0	0	2[a]	1	0
5	1[j]	1	0	1	0	0
6	0	0	0	2	1	0
			Day 7			
1	0	0	0	0	0	0
2	0[P]	0	0	0	0	0
3	0[P]	0	0	0	1	0
4	1	1	0	0	0	0
5	1	1	0	1	0	0
6	0	0	0	0	0	0

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Table 1. Individual Eye Irritation Scores (continued)

Animal No.	Cornea		Iris	Conjunctivae		
	Opacity	Involvement	Irritation	Redness	Chemosis	Discharge
			Day 14			
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	0	0	0	0	0	0
4	0	0	0	0	0	0
5	0	0	0	0	0	0
6	0	0	0	0	0	0

a Petite hemorrhaging
b Blanching
c Clear discharge
d Purulent discharge
e Hair loss around the eye
** Hair loss around the eye, possibly caused by restraint during dosing
i Injected
j Corneal epithelial peeling
p Pannus
t No pain response after test material instillation
u Excessive pawing at the treated eye after test material instillation

Positive ocular effects are summarized in Table 2. Table 3 presents the results of the sodium fluorescein examination. Six of six rabbits were positive for conjunctival redness, chemosis, corneal opacity and iridal involvement at 1 hour, but were resolved by day 14.

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Table 2. Positive[a] Ocular Effects (sexes combined) at Observation Intervals (hours)

	1	24	48	72	96	Day 7	Day 14
Cornea							
Opacity	6/6	6/6	6/6	4/6	3/6	2/6	0/6
Iris							
Iritis	6/6	6/6	5/6	3/6	0/6	0/6	0/6
Conjunctivae							
Redness	6/6	6/6	6/6	6/6	3/6	0/6	0/6
Chemosis	6/6	4/6	2/6	6	0/6	0/6	0/6

[a] The following grades for each tissue are considered positive:
Opacity (density) - Grades 1, 2, 3, and 4
Iris - Grades 1 and 2
Conjunctivae (redness) - Grades 2 and 3
Conjunctivae (chemosis) - Grades 2, 3, and 4

Table 3. Results of the Sodium Fluorescein Examinination

	Observation Period (hours)						
Sex	0	24	48	72	96	Day 7	Day 14
M	Neg	Pos (85%)	Pos (75%)	Pos (25%)	Pos (<5%)	Neg	Neg
M	Neg	Pos (45%)	Pos (10%)	Neg	Neg	Neg	Neg
M	Neg	Pos (80%)	Pos (40%)	Pos (15%)	Pos (5%)	Neg	Neg
F	Neg	Pos (5%)	Neg	Neg	Neg	Neg	Neg
F	Neg	Pos (70%)	Pos (55%)	Pos (10%)	Pos (5%)	Neg	Neg
F	Neg	Pos (30%)	Pos (10%)	Neg	Neg	Neg	Neg

Neg Negative stain retention
Pos Positive stain retention (area of cornea involved)

D. REVIEWERS' COMMENTS

Under the conditions of this study, Rejex-it AP-50 produced moderate to severe conjunctival irritation and corneal and iridal involvment in rabbits. All positive signs had resolved by day 14 post-treatment; therefore, for primary eye irritation in rabbits, Rejex-it AP-50 is classified Toxicity Category II. This study satisfies the guideline requirements (81-4) for a primary eye irritation study in rabbits.

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except for insufficient data on the test material. and may be upgraded pending submission of these data.

FINAL

DATA EVALUATION REPORT

Rejex-it AP-50

Study Type: Primary Dermal Irritation Study in Rabbits

Prepared for:

Health Effects Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
1921 Jefferson Davis Highway
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Prepared by:

Clement International Corporation
9300 Lee Highway
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January 1994

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Kate Rantz, M.P.H.

Independent Reviewer Carrie Rabe Date 1/24/94
Carrie Rabe, Ph.D.

QA Reviewer William L. McLellan Date 1/26/94
William McLellan, Ph.D.

Contract Number: 68D10075
Work Assignment Number: 3-36
Clement Number: 157
Project Officer: Caroline Gordon

Guideline Series 81-5: Primary Dermal Irritation Study in Rabbits

EPA Reviewer: J. Thomas McClintock
Biological Section, Science Analysis Branch
Health Effects Division

Signature: J. Thomas McClintock
Date: 2/9/94

EPA Section Head: Roy Sjoblad
Biological Section, Science Analysis Branch
Health Effects Division

Signature: Roy S. Sjoblad
Date: 4/11/94

Core classification
upgrading study
to guideline.

DATA EVALUATION REPORT

STUDY TYPE:	Guideline series 81-5; primary dermal irritation study in rabbits
CAS NUMBER:	
TOX CHEM NUMBER:	
MRID NUMBER:	426087-05
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it AP-50
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305704
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Primary Dermal Irritation Study of Rejex-it AP-50 in Rabbits
AUTHOR:	Steven M. Glaza
STUDY COMPLETED:	June 5, 1992
QUALITY ASSURANCE:	The test was performed under Good Laboratory Practice Standards. A Quality Assurance Statement signed June 5, 1992, was submitted.
CONCLUSIONS:	Dermal application of Rejex-it AP-50 under 4-hour semi-occluded conditions produced very slight edema in one rabbit. The average of the 4-, 24-, 48-, and 72-hour irritation scores was 0.1; therefore the test material is considered to be slightly irritating under these conditions.

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Guideline Series 81-5: Primary Dermal Irritation Study in Rabbits

CORE CLASSIFICATION: Core Supplementary. This study satisfies the guideline requirements (81-5) for a primary dermal irritation study in rabbits. However, data describing the test material were lacking (e.g., purity, stability, and lot number/identification number). This study may be upgraded pending submission of these data.

CORE GUIDELINE: PRD

TOXICITY CATEGORY: IV (Caution)

A. MATERIALS

Test Compound

Test material:	Rejex-it AP-50
Identification no.:	Lot number 56-612-69-02
Purity:	Determined by sponsor
Physical description:	White powder
Storage condition:	Room temperature
Stability:	Determined by sponsor
Dose level:	0.5 g moistened with an unspecified amount of 0.9% saline

Test Animals

Species:	Albino rabbits
Strain:	Hra:(NZW)SPF
Source:	Hazleton Research Products, Inc., Kalamazoo, MI
Sex:	3 males and 3 females
Age:	Adult
Mean body weights:	2140-2292 g for males; 2168-2418 g for females
No. animals:	3/sex/dose
Temperature:	20-22°C
Relative humidity:	40-45%
Photoperiod:	12-hour dark/12-hour light
Feeding:	Purina High Fiber Rabbit Chow #5326, measured amount daily
Water:	*Ad libitum*
Acclimation period:	At least 7 days
Housing:	Individual
Identification:	Ear tags
Selection:	Healthy animals with unspecified weight limits were selected

B. TEST PERFORMANCE

Test Material Application

The back and flanks of each rabbit were clipped free of hair the day before application. The test material, 0.5 g moistened with an unspecified amount of 0.9% saline, was applied to the intact clipped skin of each animal. A semi-occluded dressing was provided by covering the treated area with a 2.5 cm X 2.5 cm gauze patch fastened with paper tape, loosly wrapping the area in Saran wrap, and securing the dressing

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with Elastoplast tape. After 4 hours of exposure, the patch and wrappings were removed and the test sites were washed with tap water and dried with disposable paper towels.

Observation Period

The degree of erythema and edema at the test site were determined about 30 minutes after removal of the test material and recorded as the 4-hour score. Additional examinations were made at 24, 48, and 72 hours.

Scoring System

The Draize scoring system for primary dermal irritation was used.

C. RESULTS

Table 1 presents a summary of dermal irritation scores.

Table 1. Summary of Positive[a] Dermal Irritation Scores (sexes combined) (Draize Technique)

	Observation Intervals (hours)			
	4	24	48	72
Erythema	0/6	0/6	0/6	0/6
Edema	1/6	0/6	0/6	0/6

[a] The following dermal irritations scores were considered positive:
Erythema - Grades 1, 2, 3, and 4
Edema - Grades 1, 2, 3, and 4

Very slight edema was observed in only 1 rabbit. The average primary dermal irritation score was 0.2 at 4 hours and 0 at 24, 48, and 72 hours. The average of the 4-, 24- 48- and 72-hour scores was 0.1, which is considered slightly irritating. Based on these findings, Rejex-it AP-50 is classified as Toxicity Category IV (Caution).

D. REVIEWERS' COMMENTS

Rejex-it AP-50 was very slightly irritating when applied to the skin of rabbits under the 4-hour semi-occluded conditions of this study. Based on these findings, for primary dermal irritation Rejex-it AP-50 was classified Toxicity Category IV (Caution).

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FINAL

DATA EVALUATION REPORT

Rejex-it AP-50

Study Type: Dermal Sensitization Study in Guinea Pigs

Prepared for:

Health Effects Division
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U.S. Environmental Protection Agency
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Guideline Series 81-6: Dermal Sensitization Study in Guinea Pigs

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Date: 4/14/94

DATA EVALUATION REPORT

STUDY TYPE:	Guideline series 81-6; dermal sensitization study in guinea pigs
CAS NUMBER:	
TOX CHEM NUMBER:	
MRID NUMBER:	426087-06
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it AP-50
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305712
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Dermal Sensitization Study of Rejex-it AP-50 in Guinea Pigs – Closed Patch Technique
AUTHOR:	Steven M. Glaza
STUDY COMPLETED:	July 27, 1992
QUALITY ASSURANCE:	The test was performed under Good Laboratory Practice Standards. A Quality Assurance Statement, signed July 27, 1992, was submitted.
CONCLUSIONS:	Delayed contact hypersensitivity was not observed in guinea pigs exposed to Rejex-it AP-50 under the conditions of this test. The test material was not considered to be a dermal sensitizer.
CORE CLASSIFICATION:	Core Supplementary. This study satisfies the guideline requirements (81-6) for a dermal sensitization study in guinea pigs. However, data

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describing the test material were lacking (e.g., purity, stability, and lot number/identification number). This study may be upgraded pending submission of these data.

TOXICITY CATEGORY: Not applicable

A. MATERIALS

Test Compound

Test material:	Rejex-it AP-50
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	White powder
Storage condition:	Room temperature
Stability:	Determined by sponsor
Positive control material:	2,4-dinitrochlorobenzene (DNCB) (lot number 80H0121; 99.9% pure)
Naive control material:	Rejex-it AP-50 (animals treated at challenge only)
Irritation screening conc.:	Four animals each received two different concentrations of the test material, either as a 0.2 g dose (moistened with deionized water) or in 25%, 50%, or 75% w/v in 0.4 mL mineral oil.
Main study test material conc.:	Induction and challenge - 0.2 g Rejex-it AP-50 (moistened with deionized water)

Test Animals

Species:	Albino guinea pigs
Strain:	Haz:(DH)fBR
Source:	Hazleton Research Products, Inc., Denver, PA
Sex:	25 males and 3 females
No./group:	4 in irritation screening group (1 male; 3 females); 10 males in test group, 10 males in naive control group; 4 males in positive control group
Age:	Young adult
Body weights:	352-418 g, males; 368-458 g, females
Temperature:	14-25°C
Relative humidity:	30-66%
Photoperiod:	12-hour light/12-hour dark cycle
Feeding:	Purina Certified Guinea Pig Chow #5026, *ad libitum*
Water:	*Ad libitum*
Acclimation period:	At least 7 days
Housing:	Individual
Identification:	Ear tags
Selection:	Healthy animals within unspecified body weight limits were selected

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B. TEST PERFORMANCE

Skin Preparation

The hair on the back of each animal in the test and positive control groups was removed with electric clippers the day of test material application. Animals were depilated with Neet® 3 hours prior to the 24-hour examination.

Induction Phase

(a) Route of administration: The test material (0.2 g moistened with an unspecified amount of deionized water) was applied to a 25 mm diameter adhesive patch. The patch was placed on the test site (anterior left flank), covered with dental dam, and wrapped with Elastoplast tape. The patch was removed after 6 hours and the test site cleaned with a wet paper towel.

(b) Solutions used: Test group - 0.2 g (moistened with deionized water) test material; positive control group - 0.4 mL of 0.3% w/v DNCB in 80% v/v ethanol in deionized water; naive irritation control - untreated.

(c) Frequency of exposure: Test and positive control groups - 1 application per week for 3 weeks for a total of 3 applications.

(d) Duration of exposure: 6 hours

(e) Rest period: 2 weeks

(f) Observation period: 24 and 48 hours after each exposure

Challenge Phase

(a) Route of administration: Administration was the same as for the induction phase, except that the test material was placed on the right flank. The naive irritation control group of 10 was also given the challenge dose of 0.2 g test material moistened with deionized water.

(b) Solutions used: Test group and naive irritation control groups - 0.2 g test material; positive control group - 0.1% w/v DNCB in acetone.

(c) Duration of exposure: 6 hours

(d) Number of exposure: 1

(e) Observation period: 24 and 48 hours after each application

Scoring System

A modification of the Buehler method was used.

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C. RESULTS

Body weights

Body weight gain was normal in all animals.

Skin reactions

No dermal reactions were observed in the test group animals during induction or challenge with the test material. None of the animals from the naive control group reacted to the challenge application of the test material.

Mortality

No deaths occurred during the study period.

Clinical signs

No overt signs of toxicity were observed.

D. REVIEWERS' COMMENTS

A dermal sensitization reaction was not observed under the present study conditions in guinea pigs treated with Rejex-it AP-50. The test material was not considered to be a dermal sensitizer.