1-25-94

FINAL

DATA EVALUATION REPORT

Rejex-it MA

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 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: 159
Project Officer: Caroline Gordon

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

Signature: J. Thomas McClintock
Date: 7/7/94

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

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

DATA EVALUATION REPORT

STUDY TYPE:	Guideline series 81-1; acute oral toxicity in rats
CAS NUMBER:	
TOX CHEM NUMBER:	
MRID NUMBER:	426088-02
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it MA
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305693
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Acute Oral Toxicity Study of Rejex-it MA in Rats
AUTHOR:	Steven M. Glaza
STUDY COMPLETED:	July 22, 1992
QUALITY ASSURANCE:	The test was performed under Good Laboratory Practice Standards. A Quality Assurance Statement, signed July 22, 1992, was submitted.
CONCLUSIONS:	Estimated acute oral LD_{50} for males: 3633 mg/kg body weight Estimated acute oral LD_{50} for females: 3000 mg/kg body weight Estimated acute oral LD_{50} for the sexes combined: 3288 mg/kg body weight

CORE CLASSIFICATION: Core Supplemental. This study satisfies the guideline requirements (81-1) for an acute oral toxicity study in rodents. 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.

TOXICITY CATEGORY: III (Caution)

A. MATERIALS

Test Compound

Test material:	Rejex-it MA
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	Clear, pale-yellow liquid
Storage condition:	Room temperature
Bulk density:	1.15 g/mL
Stability:	Determined by sponsor
Vehicle:	None
Dose levels:	1000, 3000, and 4000 (females only) or 5000 (males only) mg/kg body weight

Controls

There were no controls.

Test Animals

Species:	Albino rat
Strain:	Crl:CD®BR
Source:	Charles River Laboratories, Inc., Portage, MI
Sex:	15 males and 15 females
Age:	Young adult
Initial body weights (fasted):	216-300 g for males; 202-244 g for females
No. animals:	5/sex/dose
Temperature:	17-28°C
Relative humidity:	24-64%
Photoperiod:	12-hour dark/12-hour light 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 body 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 conducted daily and mortality checks twice daily thereafter for 14 days.
Body weight interval:	Day 0 (before dosing), day 7, and day 14 (study termination)
Gross pathology:	Yes
Histopathology:	No

C. RESULTS

Mortality

Mortality results are summarized in Table 1. All treatment-related deaths occurred within 2 days of treatment.

Table 1. Mortality Ratios

Dosage (mg/kg)	Mortality Ratio
Males	
1000	0/5
3000	1/5
5000	5/5
Females	
1000	0/5
3000	3/5
4000	4/5

Clinical observations

Clinical signs of toxicity included the following: hypoactivity in males at all dose levels and in mid- and high-dose females: absence of

righting reflex in 5000 mg/kg males (1/5); absence of pain reflex in 4000 mg/kg females (2/5); staggered gait in 4000 mg/kg females (3/5) and 5000 mg/kg males (1/5); prostration in 4000 mg/kg females (1/5); red-stained urine in 4000 mg/kg females (1/5), and lacrimation in 3000 mg/kg females (1/5). All clinical signs resolved by day 2.

Body weights

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

Gross necropsy

Necropsy revealed dark-brown areas of variable size in the glandular mucosa of the stomachs of 1 male and 2 female rats, which died following dosing with 3000 mg/kg of the test material. It is unclear whether these areas represented treatment-related effects or were due to post-mortem changes.

LD_{50} determination

LD_{50}s were calculated using a modified Behrens-Reed-Muench cumulant method. The estimated acute oral LD_{50} for males was >3633 mg/kg body weight, 95% confidence limits 2516-5248 mg/kg. The estimated acute oral LD_{50} for females was 3000 mg/kg body weight, 95% confidence limits 1907-4719 mg/kg. The estimated acute oral LD_{50} for the sexes combined was 3288 mg/kg body weight, 95% confidence limits 2489-4343 mg/kg. The acute oral LD_{50} for males, females, and the sexes combined corresponds to Toxicity Category III (Caution).

D. REVIEWERS' COMMENTS

The estimated acute oral LD_{50s} for rats fed Rejex-it MA under these study conditions were 3633, 3000, and 3288 mg/kg body weight for males, females, and the sexes combined, respectively. These LD_{50s} correspond to Toxicity Category III (Caution).

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FINAL

DATA EVALUATION REPORT

Rejex-it MA

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
Fairfax, VA 22031

January 1994

Principal Reviewer: Kate Rantz, M.P.H. Date 1/24/94

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: 160
Project Officer: Caroline Gordon

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. S. Sjoblad
Date: 4/21/94

DATA EVALUATION REPORT

STUDY TYPE:	Guideline series 81-2; acute dermal toxicity in rabbits
CAS NUMBER:	
TOX CHEM NUMBER:	
MRID NUMBER:	426088-03
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it MA
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305697
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Acute Dermal Toxicity Study of Rejex-it MA 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 Slight dermal irritation was observed.

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CORE CLASSIFICATION: Core Supplemental. This study satisfies the guideline requirements (81-2) for an acute dermal toxicity 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.

TOXICITY CATEGORY: III (Caution)

A. MATERIALS

Test Compound

Test material:	Rejex-it MA
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	Clear, pale yellow liquid
Storage condition:	Room temperature
Stability:	Determined by sponsor
Vehicle:	None
Dose level:	2000 mg/kg body weight (as received); limit dose

Controls

There were no controls.

Test Animals

Species:	Albino rabbit
Strain:	Hra:(NZW)SPF
Source:	Hazleton Research Products, Inc., Kalamazoo, MI
Sex:	5 males and 5 females
Age:	Young adult
Initial body weights (fasted):	2146-2356 g for males; 2096-2394 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:	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

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 applied to the intact skin of the rabbit. The area of application was covered with a 10 cm X 10 cm gauze patch

secured with paper tape and overwrapped 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.

Observation period

Observations for clinical signs of toxicity and mortality 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 (Draize technique) was approximately 30 minutes after removal of the test material; subsequent readings were made days 3, 7, 10, and 14.

Body weight interval

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

Gross pathology: Yes
Histopathology: No

C. RESULTS

Mortality

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

Clinical observations

No overt signs of toxicity were observed. Slight erythema (Draize score 1) was observed in all animals. Slight edema (Draize score 1) was observed in 2 males and 2 females. The erythema was resolved in all animals by day 14. The edema was observed only at the first observation (30 minutes after removal of the test material).

Body weights

All rabbits had gained weight by study termination. However, minor (1-6%) weight loss was observed in 4 males and 2 females between days 7 and 14.

Gross necropsy

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

LD_{50} determination

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

D. REVIEWERS' COMMENTS

The estimated acute dermal LD_{50} for male and female rabbits exposed to Rejex-it MA under these study conditions was >2000 mg/kg body weight, which corresponds to Toxicity Category III (Caution). Only slight erythema and edema (Draize score 1) were observed at the test site. The dose level used in this study met the limit dose designated in the guideline.

FINAL

DATA EVALUATION REPORT

Rejex-it MA

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 1/24/94
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: 161
Project Officer: Caroline Gordon

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Guideline Series 81-4: Primary Eye 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: 4/4/94

DATA EVALUATION REPORT

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

CAS NUMBER:

TOX CHEM NUMBER:

MRID NUMBER: 426088-04

PC NUMBER: 128725

TEST MATERIAL: Rejex-it MA

SYNONYM(S): Methyl anthranilate (active ingredient)

SPONSOR: ERM Program Management Company
McLean, Virginia

STUDY NUMBER: HWI 20305705

TESTING FACILITY: Hazleton Wisconsin, Inc.
Madison, Wisconsin

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

AUTHOR: Steven M. Glaza

STUDY COMPLETED: June 16, 1992

QUALITY ASSURANCE: The test was performed under Good Laboratory Practice Standards. A Quality Assurance Statement, signed June 16, 1992, was submitted.

CONCLUSIONS: Under these study conditions, Rejex-it MA produced slight to moderate conjunctival irritation (Draize scores 0-2) to rabbit eyes, which cleared within 72 hours of treatment.

CORE CLASSIFICATION: Core Supplemental. The data describing the test material were insufficient (i.e., lot number, purity, and stability were not reported). This

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study may be upgraded pending submission of these data.

TOXICITY CATEGORY: III (Caution)

A. MATERIALS

Test Compound

Test material:	Rejex-it MA
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	Clear, pale-yellow liquid; pH not determined
Storage condition:	Room temperature
Stability:	Determined by sponsor
Vehicle:	None
Dose level:	0.1 mL (as received)

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:	2146-2312 g for males; 2188-2292 g for females
No. animals:	3/sex/dose
Temperature:	20-22°C
Relative humidity:	40-60%
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:	Animals without ocular injury or irritation were selected

B. TEST PERFORMANCE

Test Material Application

Eyes were examined the day before application using sodium fluorescein dye. The undiluted test material (0.1 mL) 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 1, 24, 48, and 72 hours after treatment according to the Draize technique.

Scoring System

Eyes were examined and scored for ocular lesions using the Draize scoring system. At 72 hours after treatment, a sodium fluorescein examination was performed to help assess corneal injury.

C. RESULTS

Individual eye irritation scores are presented in Table 1 and positive ocular effects are presented in Table 2. Corneal epithelial peeling was observed at 1, 24, and 48 hours in 3/6 animals. Blanching and clear conjunctival discharge were observed in 5/6 and 6/6 animals, respectively, at 1 hour. All signs were clear at 72 hours.

The results of the sodium fluorescein examination were negative in all rabbits before dosing and at 72 hours post-treatment. Based on these findings, the primary eye irritation potential of Rejex-it MA was classified as Toxicity Category III (Caution).

Table 1. Individual Eye Irritation Scores According to the Draize Technique

Animal No.	Cornea		Iris	Conjunctivae		
	Opacity	Involvement	Irritation	Redness	Chemosis	Discharge
			1 hour			
1[u]	1[j]	1	1[i]	2[b]	2	2[c]
2[u]	1[j]	1	1[i]	2[b]	2	2[c]
3[u]	0	0	1[i]	2[b]	2	2[c]
4[u]	0	0	1[i]	2[b]	2	2[c]
5[u]	1	1	0	1	1	1[c]
6[u]	0	0	0	2[b]	2	2[c]
			24 hours			
1	1[j]	2	0	2	1	0
2	1[j]	1	0	1	1	0
3	0	0	0	1	1	0
4	1[j]	2	0	2	2	1[c]
5	0	0	0	1	0	0
6	0	0	0	1	0	0
			48 hours			
1	1[j]	1	0	2	1	0
2	1[j]	1	0	1	0	0
3	0	0	0	1	0	0
4	1[j]	1	0	2	1	0
5	0	0	0	1	0	0
6	0	0	0	1	0	0
			72 hours			
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

[b] Blanching
[c] Clear discharge
[i] Injected
[j] Corneal epithelial peeling
[u] Excessive pawing at the treated eye after test material instillation

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Table 2. Summary of Positive[a] Ocular Effects (sexes combined)

	Observation Intervals (hours)			
	1	24	48	72
Cornea				
Opacity	3/6	3/6	3/6	0/6
Iris				
Iritis	4/6	0/6	0/6	0/6
Conjunctivae				
Redness	5/6	2/6	2/6	0/6
Chemosis	5/6	1/6	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

D. REVIEWERS' COMMENTS

Rejex-it MA produced slight to moderate cojunctival irritation (Draize scores 0-2) and corneal and iridal involvement (i.e., scattered or diffuse corneal opacity and circumcorneal injection in the iris) in the eyes of rabbit under conditions of this study. All positive signs were clear by 72 hours; therefore, the primary eye irritation potential of Rejex-it MA is Toxicity Category III (Caution). This study satisfies the guideline requirements (81-4) for a primary eye irritation study in rabbits; however, certain information on the lot number, purity, and stability of the test material was not provided.

FINAL

DATA EVALUATION REPORT

Rejex-it MA

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
Arlington, VA 22202

Prepared by:

Clement International Corporation
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January 1994

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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: 162
Project Officer: Caroline Gordon

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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 D. Sjoblad
Date: 2/14/94

DATA EVALUATION REPORT

STUDY TYPE:	Guideline series 81-5; primary dermal irritation study in rabbits
CAS NUMBER:	
TOX CHEM NUMBER:	
MRID NUMBER:	426088-05
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it MA
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305701
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Primary Dermal Irritation Study of Rejex-it MA 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 MA under 4-hour semi-occluded conditions produced no dermal irritation. Under the conditions of this test, Rejex-it MA is considered non-irritating.
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.

TOXICITY CATEGORY: IV (Caution)

A. MATERIALS

Test Compound

Test material:	Rejex-it MA
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	Clear, pale-yellow liquid; pH not determined
Storage condition:	Room temperature
Stability:	Determined by sponsor
Vehicle:	None
Dose level:	0.5 mL (as received)

Test Animals

Species:	Albino rabbits
Strain:	Hra:(NZW)SPF
Source:	Hazleton Research Products, Inc., Kalamazoo MI
Sex:	3 males and 3 females
Age:	Adult
Initial body weights:	2206-2294 g for males; 2182-2278 g for females
No. animals:	3/sex/dose
Temperature:	20-22°C
Relative humidity:	40-45%
Photoperiod:	12-hour light/12-hour dark 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 an unspecified body weight range were selected

B. TEST PERFORMANCE

Test Material Application

The back and flanks of each rabbit were clipped the day before application of the test material. The test material (0.5 mL) was applied to the intact clipped skin of each animal, and the treated area was covered with a 2.5 cm X 2.5 cm gauze patch, which was fastened with paper tape, loosly wrapped in Saran Wrap, and secured with Elastoplast tape to provide a semi-occlusive dressing. 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 was recorded as the 4-hour score. Additional examinations were made at 24, 48, and 72 hours. The Draize scoring system for primary dermal irritation was used.

C. RESULTS

A summary of dermal irritation scores is presented in Table 1.

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	0/6	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

No erythema or edema was observed at any time. Based on these findings, Rejex-it MA was considered nonirritating and classified Toxicity Category IV (Caution).

D. REVIEWERS' COMMENTS

Rejex-it MA was found to be nonirritating when applied to the skin of rabbits under the 4-hour semi-occluded conditions of this study. As a primary dermal irritant, Rejex-it MA was classified Toxicity Category IV (Caution).

FINAL

DATA EVALUATION REPORT

Rejex-it MA

Study Type: Dermal Sensitization Study in Guinea Pigs

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

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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: 163
Project Officer: Caroline Gordon

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Guideline Series 81-5: Dermal Sensitization Study in Guinea Pigs

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 F. Sjoblad
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:	426088-06
PC NUMBER:	128725
TEST MATERIAL:	Rejex-it MA
SYNONYM(S):	Methyl anthranilate (active ingredient)
SPONSOR:	ERM Program Management Company McLean, Virginia
STUDY NUMBER:	HWI 20305709
TESTING FACILITY:	Hazleton Wisconsin, Inc. Madison, Wisconsin
TITLE OF REPORT:	Dermal Sensitization Study of Rejex-it MA 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 MA under the conditions of this test.
CORE CLASSIFICATION:	Core Supplementary. This study satisfies the guideline requirements (81-6) for a dermal sensitization study in guinea pigs. However, data describing the test material were lacking (e.g.,

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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 MA
Identification no.:	Not reported
Purity:	Determined by sponsor
Physical description:	Clear, pale-yellow liquid
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 MA (animals treated at challenge only)
Irritation screening conc.:	Four animals each received two different concentrations of the test material, either undiluted or in 25%, 50%, or 75% w/v in mineral oil.
Main study test material conc.:	Induction and challenge - 0.4 mL Rejex-it MA

Test Animals

Species:	Albino guinea pigs
Strain:	Haz:(DH)fBR
Source:	Hazleton Research Products, Inc., Denver, PA
Sex:	19 males and 9 females
No./group:	4 in irritation screening group (1 male, 3 females); 10 in test group (8 males, 2 females); 10 in naive control group (8 males, 2 females); 4 in positive control group (2 males, 2 females)
Age:	Young adult
Mean body weights:	430-542 g, males; 398-542 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 depilatated with Neet® 3 hours prior to the 24-hour examination.

Induction Phase

(a) Route of administration: The test material (0.4 mL) 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 - 0.4 mL test material; positive control group - 0.4 mL 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 0.4 mL test material.

(b) Solutions used: Test group and naive irritation control groups - 0.4 mL test material; positive control group - 0.4 mL 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 application

Scoring System

A modification of the Buehler method was used.

C. RESULTS

Clinical signs

No overt signs of toxicity were observed in treated rabbits.

Skin reactions

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

Body weights

Body weight gain was normal in all animals, except in the single animal sacrificed moribund.

Mortality

One animal from the naive control group was sacrificed moribund on day 23. This animal appeared thin on days 15-23, had soft stool on day 16, few feces on days 17-23, lost 172 g body weight the first 21 days of the study, and was sacrificed on day 23.

D. REVIEWERS' COMMENTS

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