06/25/2001

008663

MEMORANDUM:

Subject: EPA File Symbol/EPA Reg. No.: [10182-GEG] ERADICANE 25G

MJP 6-11-01

From: Mark J. Perry, Biologist
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

To: Robert J. Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (H7505C)

Thru: Thomas C. Ellwanger, Section Head
Precautionary Review Section
Registration Support Branch
Registration Division (H7505C)

= 6/25/01

Applicant: ICI Americas Inc.
Concord Pike & New Murphy Road
Wilmington, DE 19897

FORMULATION FROM LABEL:

	% by wt.
435 Active Ingredient(s): S-ethyl dipropylthiocarbamate.....	25.0
Inert Ingredient(s):	75.0
Total:	100%

1/13

BACKGROUND ICI Americas has submitted acute oral, acute dermal, eye irritation, dermal irritation, and dermal sensitization studies for review. The product is ERADICANE 25G, a selective herbicide, and the active ingredient is S-ethyl dipropylthiocarbamate [25.0%]. All studies were performed by ICI and the MRID numbers are 418312-01 through 418312-05.

RECOMMENDATION

[1] The acute oral toxicity, eye irritation, dermal irritation, and dermal sensitization studies are acceptable and have been graded core guideline. The acute dermal toxicity study is acceptable and has been graded core minimum.

a) The Guidelines state that the test animals should weigh between 200 and 300 grams. All of the male test animals were outside this weight range, therefore, this study has been graded core minimum.

[2] The registrant must submit an acute inhalation toxicity study, or a formal waiver request supported by sound scientific rationale and the results of efforts to mill the product.

LABELING

[1] The appropriate signal word is CAUTION.

[2] The precautionary statements should read as follows:

Harmful if absorbed through skin. Causes eye irritation. Avoid contact with skin, eyes or clothing. Wash thoroughly with soap and water after handling.

[3] The statements of practical treatment should read as follows:

IF IN EYES: Flush with plenty of water. Call a physician if irritation persists.

IF ON SKIN: Wash with plenty of soap and water. Get medical attention.

[4] Delete the statement "Harmful If Swallowed" below the signal word.

[5] Further labeling revisions may be required upon submission of additional study data.

ACUTE TOXICITY PROFILE

Acute Oral	Category 4/Guideline
Acute Dermal	Category 3/Minimum
Acute Inhalation	Not submitted
Eye Irritation	Category 3/Guideline
Dermal Irritation	Category 4/Guideline
Dermal Sensitization	Negative /Guideline

008663

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§ 81-1)

Product Manager: 25
MRID No.: 418312-01
Testing Facility: ICI Central Tox. Labs.
Author(s): D. Lees, A.M. Leah
Species: Rat
Age: Young Adult
Weight: 198-315 g
Source: Barriered A.B.U.
Test Material: Eradicane 25G
Quality Assurance (40 CFR §160.12): Present

Reviewer: M. Perry
Report Date: 6-7-91
Report No.: AR5141

Conclusion:

1. LD_{50} (mg/kg): Males = --
   Females = --
   Combined = --
2. The estimated LD_{50} is > 5.0 g/kg
3. Tox. Category: 4 **Classification:** Guideline

Procedure (Deviations from §81-1):

Results:

Dosage g/kg	(Number Killed/Number Tested)		
	Males	Females	Combined
5.0	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings: Nine of ten animals surpassed their pre-dose weight by study termination. Clinical signs of toxicity included piloerection, upward curvature of the spine, and irregular breathing [n=2]. No abnormalities were observed upon necropsy.

008663

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: 25 **Reviewer:** M. Perry
MRID No.: 418312-02 **Report Date:** 6-7-91
Testing Laboratory: ICI Central Tox. Labs. **Report No.:** CR2823
Author(s): D. Lees, A.M. Leah
Species: Rat
Weight: Females:218-243g, Males:335-382g
Source: Barriered A.B.U.
Test Material: Eradicane 25G
Quality Assurance (40 CFR §180.12): Present

Summary:

1. LC_{50} (mg/kg): Males = --
   Females = --
   Combined = --

2. The estimated LD_{50} is > 2.0 g/kg

3. Tox. Category: 3 Classification: Minimum

Procedure (Deviation From §81-2): All of the male test animals were outside the weight limit specified in the guidelines.

Results:

Reported Mortality

DOSAGE ς/kg	(NUMBER KILLED/NUMBER TESTED)		
	Males	Females	Combined
2.0	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings: Nine of ten animals surpassed their pre-dose weights by study termination. No significant abnormalities were noted during clinical exams or necropsy.

008663

ORAL TOXICITY DATA SHEET

EPA REG.# 10182-GEG

MRID # 418312-01

ANIMAL [RAT]	✓	
AGE [YOUNG ADULT]	✓	
5/SEX/DOSE LEVEL	✓	One dose level
LIMIT TEST	✓	5.0 g/kg
FASTED	✓	24 hrs prior
METHOD OF ADMINISTRATION	✓	Gavage w/ plastic catheter
DOSE CONC & DOSE LEVELS	✓	above
OBSERVATION PERIOD & FREQUENCY	✓	15 day, once daily
BODY WEIGHT FREQUENCY & RESULTS	✓	-1, 1, 3, 6, 8, 15 / 9 of 10 gained
MORTALITY CHART & LD-50	✓	All survived
CLINICAL EXAM RESULTS	✓	In 2 animals: piloerection, upward curv, irreg breathing
NECROPSY RESULTS	✓	No ab [illegible]

DERMAL TOXICITY DATA SHEET

EPA REG.# 10182-GEG

MRID# 41831 2-02

ANIMAL ~~[RABBIT]~~	✓	Rat
TEST MATERIAL PREPARATION	✓	Moistened w/ d_2H_2O (0.3 - 0.4 mL)
5/SEX/DOSE LEVEL	✓	
LIMIT TEST	✓	2g/Kg
CLIPPED	✓	
METHOD OF APPLICATION	✓	
METHOD OF OCCLUSION	✓	gauze + occ dressings
BODY WEIGHT FREQUENCY & RESULTS	✓	days 1,3,4,8,15 / All gained but one
DOSE CONC & DOSE LEVELS	✓	
EXPOSURE TIME	✓	24 hrs
REMOVAL OF EXCESS MATERIAL	✓	wash
MORTALITY CHART & LD-50	✓	All survived
CLINICAL EXAM RESULTS	✓	No significant
NECROPSY RESULTS	✓	

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (§81-4)

Product Manager: 25
MRID No.:418312-04
Testing Laboratory: ICI Central Tox. Labs.
Author(s): D. Lees, P. Robinson
Species: Rabbit
Sex: --
Weight: 2935-3591 g
Source: Mellor Rabbitry
Dosage: 100 mg
Test Material: Eradicane 25G
Quality Assurance (40 CFR §160.12): Present

Reviewer: M. Perry
Report Date: 6-7-91
Report No.: FB4432

Summary:

1. **Toxicity Category:** 3
2. **Classification:** Guideline

Procedure (Deviations From §81-4):

Results:

Observations	(number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity	0/6	1/6	1/6	1/6	0/3			
Iris	0/6	0/6	0/6	0/6	0/3			
Conjunctivae								
Redness	4/6	3/6	1/6	0/6	0/3			
Chemosis	2/6	1/6	0/6	0/6	0/3			
Discharge								

Comments: Corneal involvement and irritation cleared by day seven in all animals.

EYE IRRITATION DATA SHEET

EPA REG.# 10182-GEG

MRID# 418312-04

ANIMAL [RABBIT]	✓	
DOSE VOLUME ~~[0.1ml]~~	✓	100 mg
TEST MATERIAL DESCRIPTION	✓	brown solid
METHOD OF ADMINISTRATION	✓	placed into conj sac
DOSE CONC	✓	undiluted
OBSERVATION PERIOD & FREQUENCY	✓	3-7 days
OBSERVATION METHOD	✓	fluorescein dye
EVALUATION RESULTS	✓	Grade 1-2 erythema + chemosis, Grade 1 opacity (n=1) [redacted]

208663

DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: 25
MRID No.: 416312-03
Testing Laboratory: ICI Central Tox. Labs.
Author(s): D. Lees, P. Robinson
Species: Rabbit
Age: Young Adult
Sex: --
Weight: --
Dosage: 500 mg
Test Material: Eradicane 25G
Quality Assurance (40 CFR §160.12): Present

Reviewer: M. Perry
Report Date: 6-7-91
Report No.: EB3905

Summary:

1. **The Primary Irritation Index** = < 0.5
2. **Toxicity Category:** 4
3. **Classification:** Guideline

Procedure (Deviations From §81-5):

Results: One test animal exhibited grade one erythema and edema until study day three.

Special Comments:

SKIN IRRITATION DATA SHEET

EPA REG.# 10182-GEG

MRID# 418312-03

ANIMAL [RABBIT]	✓	6
DOSE VOLUME [~~0.5ml~~]	✓	500mg
DOSE CONC	✓	
CLIPPED	✓	
TEST MATERIAL DESCRIPTION	✓	solid moistened w/ 0.4 ml dH2O
EXPOSURE TIME	✓	4hrs
EXPOSURE SITE AREA	✓	Flank
OCCLUSION	✓	Gauze + Rubber sheeting
POST-EXPOSURE WASH	✓	
OBSERVATION PERIOD & FREQUENCY	✓	72 hrs - 7 days
EVALUATION RESULTS	✓	One animal exhibited grade 1 erythema + edema

008663

DATA REVIEW FOR SKIN SENSITIZATION TESTING (§81-6)

Product Manager: 25
MRID No.: 418312-05
Testing Laboratory: ICI Central Tox. Labs.
Author(s): D. Lees, P. Robinson
Species: Guinea Pig
Weight: 373-530g
Source: Barriered A.B.U.
Test Material: Eradicide 25G
Positive Control Material: Formaldehyde
Quality Assurance (40 CFR §160.12): Present

Reviewer: M. Perry
Report Date: 6-7-91
Report No.: GG5149

Method: Buehler

Summary:

1. This Product is not a dermal sensitizer.

2. Classification: Guideline .

Procedure (Deviation From §81-6):

Results: No positive reactions were observed in the test [induced] or naive control animals following challenge. The positive control study was successful and verified the test method.

DERMAL SENSITIZATION DATA SHEET

EPA REG.# 10182-GEG

MRID# 418312-05

ANIMAL [GUINEA PIG]	✓	20 test 10 naive control
POSITIVE CONTROL DESCRIPTION	✓	Formaldehyde / Positive test
TEST METHOD	✓	Buehler
PRE-SCREEN RESULTS	✓	Solid moistened w/ dH_2O → 53% was highest achievable conc also non-irr
INDUCTION DESCRIPTION	✓	1 6hr induction/wk for 3 wks
EXPOSURE TIME	✓	6hrs
EXPOSURE SITES & PREP	✓	Induction: Scapular region Challenge: Flank
OCCLUSION	✓	Patch + elastic bandage
CHALLENGE DESCRIPTION	✓	Used 53% and 30% for each animal
NAIVE CONTROLS	✓	
INDUCTION RESULTS	✓	Slight erythema in some animals after 2nd induction
CHALLENGE RESULTS	✓	No irritation in test or naive animals