JUN 1 _ 1995

MEMORANDUM

Chemical: 121011 Clethodim
Reference: DP Barcode D194689

Subject: EPA File Symbol/EPA Reg. No. 059639-IG
SELECT® 37% MUP

From: S.E. Oonnithan 5/30/95
Precautionary Review Section
Registration Support Branch (H7505W)
Registration Division

To: Joanne I. Miller, PM 23
Fungicide-Herbicide Branch (H7505C)
Registration Division

Applicant: Valent U.S.A. Corporation
1333 North California Blvd., Suite: 600
Walnut Creek, CA 94596-8025

FORMULATION FROM LABEL:

Active Ingredient(s)	% by wt.
Clethodim	37.0
Inert Ingredient(s)	63.0
Total	100.0

BACKGROUND

Valent U.S.A. Corporation submitted acute toxicity studies using two herbicide formulations, SELECT® 37% MUP: acute oral toxicity (MRID No. 428654-02), acute dermal toxicity (MRID Nos. 428654-03 and 430243-01), acute inhalation toxicity (MRID No. 428743-01), primary eye irritation (MRID No. 428654-04), and primary skin irritation (MRID Nos. 428654-06 and 430243-02) studies using Sample No. SX-1860 (Basic Formula) and primary eye irritation (MRID No. 428654-05) and primary skin irritation (MRID Nos. 428654-07 and 430243-03) studies using Sample No. SX-1861 (Alternate Formula). These formulations contain different inert solvents.

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The acute toxicity studies were performed by IIT Research Institute, Chicago, IL and Hill Top Biolabs, Inc., Miamiville, OH.

RECOMMENDATION

1. Acute Oral: Supplementary. Since 2/5 animals in each sex group died in the limit test, a new study using either a 2 g/kg dose or a multiple dose LD_{50} is required.

2. Acute Dermal: Category III. The acute dermal toxicity study is acceptable.

3. Acute Inhalation: Category IV. The acute inhalation toxicity study is acceptable.

4. Eye Irritation: Category IV. The eye irritation study is acceptable.

5. Skin Irritation: Category II. The skin irritation study is acceptable.

6. Dermal Sensitization: Judged **positive** based on the data submitted under FIFRA 6[a][2] (MRID No. 422028-01; Delayed Contact Hypersensitivity in Guinea Pigs (Buehler Technique) with Clethodim 37% MUP [SX-1860]; Letter from E. Bruce to PM-23 dated 06/07/93). The registrant also stated in the proposed product label under precautionary statement, that the product may cause allergic reaction. PRS could not find a review of this study in PRS files or in the Jacket.

LABELING

The appropriate signal word is WARNING.

Recommended Precautionary Labeling:

Causes skin irritation. Harmful if absorbed through skin. Do not get on skin or clothing. Avoid contact with eyes. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.

Recommended Statements of Practical Treatment:

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

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

IF SWALLOWED: Drink promptly a large quantity of milk, egg white, gelatin solution, or if these are not available large quantities of water.

Additional precautionary labeling may be necessary following review of the required data.

COMMENTS

The eye irritation toxicity categories for Sample No. SX-1860 (Basic Formula) and Sample No. SX-1861 (Alternate Formula) are IV and III respectively; therefore the two formulas are not interchangeable. It is recommended that the registrant pick one of the two MUP formulas for registration now and submit a separate application for registration of the other formula.

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

Product Manager: 23
Reviewer: S. Oonnithan
MRID No.: 428654-02
Report No.: 91-8140-21(A)
Author(s): T.D. Morris
Report Date: 01/16/92
Testing Facility: Hill Top Biolabs, Inc.

Species: Rat
Age: Young adults
Weight: Males 242-265 g; Females 233-241 g
Source: Harlan Sprague-Dawley, Inc.

Test Material: Clethodim 37% MUP, Sample No. SX-1860.
Dosage: 5 g/kg; undiluted

Conclusion:
LD_{50}: **Males:** --
Females: --
Combined: >5 g/kg
Estimated LD_{50}: --
Tox. Category: --
Classification: Supplementary

Quality Assurance (40 CFR §160.12): Included
Procedure (Deviations from §81-1): None.

Results:

Dosage	Number Killed/Number Tested		
	Males	Females	Combined
5 g/kg	2/5	2/5	4/10

Symptoms & Gross Necropsy Findings: Clinical symptoms noted during the observation period included slight to severe depression, labored breathing, body tremors, eye squinting, dehydration, ataxia, hunched posture, piloerection, and saliva, urine, and fecal stains. All surviving animals exhibited body weight gain. Gross necropsy findings in the dead animals were generally agonal and no observable necropsy abnormalities were found in survivors.

Comments: Since 2/5 animals in each sex group died in the limit test, a new study using either a 2 g/kg dose or a multiple dose LD_{50} is required.

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

Product Manager: 23 **Reviewer:** S. Oonnithan
MRID No.: 430243-01 **Report No.:** 91-140
Author(s): W. Johnson **Report Date:** 08/27/92
Testing Facility: IIT Research Institute, Chicago, IL.

Species: Rabbit, New Zealand albino
Age: Young adult (2-4 months)
Weight: Males 2.64-3.02 kg; Females 2.56-2.95 kg
Source: Johnson Rabbit Ranch, Wilkinson, IN.

Test Material: Clethodim 37% MUP, Sample No. SX-1860.
Dosage: 2 g/kg; undiluted

Conclusion:
LD_{50}: **Males:** --
Females: --
Combined: >2 g/kg
Estimated LD_{50}: >2 g/kg
Tox. Category: III
Classification: Acceptable

Quality Assurance (40 CFR §160.12): Included
Procedure (Deviations from §81-2): None

Results:

Dosage	Number Killed/Number Tested		
	Males	Females	Combined
2 g/kg	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings:
No treatment related signs of toxicity were found in any of the animals. Dermal irritation (erythema and/or edema) was observed at the application site with superficial flaking in all test animals. Eschar formation was present in 8 out of ten animals on day 5. Only two animals recovered completely from all signs of dermal irritation by day 14. No significant gross lesions were observed at necropsy.

The registrant also submitted a second acute dermal study (MRID No. 428654-03, Hill Top Biolabs ID No. 91-8141-21[A]), which was performed using rabbits previously used for an eye irritation study for another test chemical (Letter of E.D. Bruce, dated 11/11/93 to PM 23). This study was not reviewed.

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DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3)

Product Manager: 23 **Reviewer:** S. Oonnithan
MRID No.: 428743-01 **Report No.:** L08329-L001
Author(s): S. Garthwaite **Report Date:** 10/10/91
Testing Facility: IIT Research Institute, Chicago, IL.

Species: Rat, Sprague-Dawley
Age: Young adult (≈6 weeks)
Weight: Males 286-306 g; Females 225-249 g
Source: Charles River Breeding Labs., Inc., Portage, MI.

Test Material: Clethodim 37% MUP, Sample No. SX-1860. Used undiluted.
Dosage: See below
Test Conditions: Test animals were subjected to whole body exposure in 0.5 m^3 stainless steel and glass chamber. Aerosol concentration was measured gravimetrically, Chamber air flow was maintained at 122 l/min during exposure.

Conclusion:
LD_{50}: **Males:** --
Females: --
Combined:
Estimated LD_{50}: >5.96 mg/l
Tox. Category: IV
Classification: Acceptable

Quality Assurance (40 CFR §160.12): Included
Procedure (Deviations from §81-3): None

Results:

Exposure Concentration	Number Killed/Number Tested		
	Males	Females	Combined
5.96 mg/l MMAD 2.15 μm; GSD 2.14	0/5	0/5	0/10

Symptoms & Gross Necropsy Findings:
Clinical symptoms during exposure included salivation, lacrimation, redness around nose and eyes, and wet and discolored paws and inguinal fur with diminishing severity during the observation period. All rats gained weight during the study. Necropsy findings were within normal limits in all rats.

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

Product Manager: 23
MRID No.: 428654-04
Author(s): T.D. Morris

Reviewer: S. Oonnithan
Report No.: 91-8145-21(A)
Report Date: 01/17/92

Species: Rabbit; Strain: New Zealand White
Age: Young adult
Source: Myrtle's Rabbitry.

Test Material: Clethodim 37% MUP, Sample No. SX-1860.
Dosage: 0.1 ml; undiluted
Test Conditions: The eyes were washed after 24 hours and scored with and without fluorescein staining.

Summary:
Tox. Category: IV
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included
Procedure (Deviations from §81-4): None

Results:

Observations	Number "positive"/Number tested at					
	1 Hr	24 Hrs	48 Hrs	72 Hrs	4 Days	7 Days
Cornea Opacity	0/6	0/6	0/6	0/6	--	--
Iris	0/6	0/6	0/6	0/6	--	--
Conjunctivae: Redness	3/6	0/6	0/6	0/6	--	--
Chemosis	1/6	0/6	0/6	0/6	--	--
Discharge	0/6	0/6	0/6	0/6	--	--

Comments: The conjunctival irritation cleared in 24 hours.

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

Product Manager: 23
MRID No.: 428654-05
Author(s): T.D. Morris

Reviewer: S. Oonnithan
Report No.: 91-8146-21(A)
Report Date: 01/17/92

Species: Rabbit; **Strain:** New Zealand White
Age: Young adult
Source: Myrtle's Rabbitry.

Test Material: Clethodim 37% MUP, Sample No. SX-1861.
Dosage: 0.1 ml; undiluted.
Test Conditions: The eyes were washed after 24 hours and scored with and without fluorescein staining.

Summary:
Tox. Category: III
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included
Procedure (Deviations from §81-4): None

Results:

Observations	Number "positive"/Number tested at					
	1 Hr	24 Hrs	48 Hrs	72 Hrs	4 Days	7 Days
Cornea Opacity	0/6	0/6	0/6	0/6	--	--
Iris	0/6	0/6	0/6	0/6	--	--
Conjunctivae: Redness	1/6	0/6	0/6	0/6	--	--
Chemosis	1/6	0/6	0/6	1/6	1/1	0/1
Discharge	0/6	0/6	0/6	0/6	--	--

Comments: The conjunctival irritation cleared in 4 days.

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

Product Manager: 23 **Reviewer:** S. Oonnithan
MRID No.: 430243-02 **Report No.:** 91-141
Author(s): W. Johnson **Report Date:** 10/23/92
Testing Facility: IIT Research Institute, Chicago, IL.

Species: Rabbit, New Zealand albino
Age: Young adult (2-4 months)
Weight: 2.24-2.91 kg when received.
Source: Johnson Rabbit Ranch, Wilkinson, IN.

Test Material: Clethodim 37% MUP, Sample No. SX-1860.
Dosage: 0.5 ml/site; undiluted

Summary:
Tox. Category: II
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included
Procedure (Deviations from §81-5): None

Results: All test animals had slight to severe erythema and slight to severe edema. At 72 hours, the dermal irritancy mean scores ranged from 4.0 to 6.5 with an average of averaged 5.6. At 7 days, two test animals showed signs of eschar formation and four animals showed superficial flaking at test site. Even though slight erythema and/or edema was evident in three rabbits at 14 days after testing, complete recovery from all signs of dermal irritation was evident towards the end of the study.

Comments: The registrant also submitted a second acute dermal study (MRID No. 428654-06) performed by Hill Top Biolabs, Inc. This study was not reviewed, as the registrant reported (Letter of E.D. Bruce dated 11/11/93 to PM 23) that the test rabbits were previously used for an eye irritation study for another test chemical.

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

Product Manager: 23 **Reviewer:** S. Oonnithan
MRID No.: 430243-03 **Report No.:** 91-139
Author(s): W.D. Johnson **Report Date:** 10/23/92
Testing Facility: IIT Research Institute, Chicago, IL.

Species: Rabbit, New Zealand albino
Age: Young adult (2-4 months)
Weight: 2.03-2.95 kg at arrival
Source: Johnson Rabbit Ranch, Wilkinson, IN.

Test Material: Clethodim 37% MUP, Sample No. SX-1861.
Dosage: 0.5 ml/site; undiluted

Summary:
Tox. Category: II
Classification: Acceptable
Quality Assurance (40 CFR §160.12): Included
Procedure (Deviations from §81-5): None

Results: All test animals had slight to severe erythema and slight to severe edema. At 72 hours, the mean dermal irritancy scores ranged from 3.5 to 6.3 with an average of 5.0. At 7 days, one test animal had signs of eschar formation, two had superficial flaking, and one had cracked/scaly appearance at test site. No full thickness necrosis or ulceration was observed. Even though slight erythema was present in three rabbits 14 days after testing, complete recovery from all signs of dermal irritation was evident towards the end of the study.

Comments: The registrant also submitted a second acute dermal study (MRID No. 428654-07) performed by Hill Top Biolabs, Inc. This study was not reviewed, as the registrant reported (Letter of E.D. Bruce dated 11/11/93 to PM 23) that the test rabbits were previously used for an eye irritation study for another test chemical.

ACUTE TOX ONE-LINER

1. **DP BARCODE:** D194689

2. **PC CODE(S):** 121011

3. **CURRENT DATE:** 05/30/95

4. **TEST MATERIAL:** SELECT® 37% MUP; Sample Nos. SX-1860 and SX-1861.

Study/Species/ Lab/Study#/Date	MRID No.	Results	Tox. Cat.	Core Grade [a]
81-1, Rat, Hill Top Biolabs 91-8140-21(A), 01/16/92	428654-02	--	--	S
81-2, Rabbit, IIT Research Inst. 91-140, 08/27/92	430243-01	LD_{50} >2 g/kg	III	A
81-3, Rats, IIT Research Inst. L08329-L001, 10/10/91	428743-01	LD_{50} >5.96 mg/l	IV	A
81-4, Rabbit, Hill Top Biolabs 91-8145-21(A), 01/17/92	428654-04	Conjunctival irritation cleared in 24 hours.	IV	A
81-4, Rabbit, Hill Top Biolabs 91-8146-21(A), 01/17/92	428654-05	Conjunctival irritation cleared in 4 days.	III	A
81-5, Rabbit, IIT Research Inst. 91-141, 10/23/92	430243-02	Moderate to severe erythema and moderate edema present at 72 hours	II	A
81-5, Rabbit IIT Research Inst. 91-139, 10/23/92	430243-03	Moderate to severe erythema and moderate edema present at 72 hours	II	A

[a] Core Grade Key: A = Acceptable, S = Supplementary, and U = Unacceptable.

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