(2-20-98)

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

20/FEB/1998

MEMORANDUM

Subject: EPA Reg. No: 59639-RNE
DP Barcode: D239213
Case No: 062077

From: Masih Hashim, Toxicologist MH 2.20
Technical Review Branch
Registration Division (7505C)

To: Daniel Kenny, PM Team 23
Herbicide Branch
Registration Division (7505C)

Applicant: Valent USA Corporation
1333 N. California Blvd. Ste. 600
Walnut Creek, CA 94596

FORMULATION FROM LABEL:

Active Ingredient(s):		% by wt.
121011	Clethodim	13.2
Inert Ingredient(s):		86.8
Total:		100%

BACKGROUND: Valent USA Corporation has submitted a set of six acute toxicity studies to support the registration of Select Super Herbicide. The MRID numbers are 443603-01 through 06. These studies were summarized by an Agency contractor, then evaluated and revised by TRB. All six studies were conducted mainly at the Safepharm Laboratories in Derby, UK.

RECOMMENDATION:

Each of the six studies is acceptable according to the Sub-Division F guidelines. The acute toxicology profile for the File Symbol 59639-RNE is as follows:

acute oral toxicity	IV	acceptable
acute dermal toxicity	III	acceptable
acute inhalation toxicity	IV	acceptable
primary eye irritation	IV	acceptable
primary skin irritation	III	acceptable
dermal sensitization	not a sensitizer	acceptable

LABELING:

ID #: 059639-00102 SELECT SUPER HERBICIDE

SIGNAL WORD: CAUTION

PRECAUTIONARY STATEMENTS:

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

STATEMENT OF PRACTICAL TREATMENT (SOPT):

IF ON SKIN: Wash with plenty of soap and water. Get medical attention. For Category III, add "if symptoms persist."

2

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (§81-1, 870.1100)

Product Manager: 23
MRID No.: 44360301

Reviewer: Masih Hashim
Study Completion Date: December 12, 1996
Study No.: 986/001

Testing Facility: Safepharm Laboratories, Ltd. & Tomen Agro, Inc.
Author: Driscoll, R.

Quality Assurance (40 CFR §160.12): Included

Test Material: Select® Super Herbicide TM-5403
Species: Rats; Sprague-Dawley CD
Age: 5-8 weeks
Weight: Males: 156-171 g; Females: 144-149 g

Source: Charles River (UK) Ltd, Margate, Kent

Conclusion:

1. LD_{50} (mg/kg):
   Males: >5000 mg/kg
   Females: >5000 mg/kg
   Combined: >5000 mg/kg
2. The estimated LD_{50} is >5000 mg/kg
3. Tox. Category: IV

Classification: Acceptable

Procedure (Deviations from §81-1): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
5000	0/5	0/5	0/10

Observations: No animals died during the study. All animals had hunched posture. The females had additional clinical signs which included lethargy, decreased respiratory rate, labored respiration, and increased salivation. One female had red/brown staining around the mouth. All animals recovered within two days of dosing and had normal body weight gains.

Gross Necropsy: No abnormalities were found.

3

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2, 870.1200)

Product Manager: 23
MRID No.: 44360302

Reviewer: Masih Hashim
Study Completion Date: December 12, 1996
Study No.: 986/002

Testing Facility: Safepharm Laboratories, Ltd. & Tomen Agro, Inc.
Author: Driscoll, R.

Quality Assurance (40 CFR §160.12): Included

Test Material: Select® Super Herbicide TM-5403
Species: Rats; Sprague-Dawley
Age: Approximate 10-14 weeks
Weight: Males: 223-234 g; Females: 207-234 g

Source: Charles River (UK) Ltd, Margate, Kent

Dermal LD_{50} Testing:

Conclusion:

1. LD_{50} (mg/kg):
   Males: >2000 mg/kg
   Females: >2000 mg/kg
   Combined: >2000 mg/kg
2. The estimated LD_{50} is >2000 mg/kg
3. Tox. Category: III Classification: Acceptable

Procedure (Deviations from §81-2): None

Results:

Dosage (mg/kg)	Number of Deaths/Number Tested		
	Males	Females	Combined
2000	0/5	0/5	0/10

Observations: No animals died during the study. All animals appeared healthy and had normal body weight gains.

Gross Necropsy: No abnormalities were found.

4

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (§81-3, 870.1300)

Product Manager: 23
MRID No.: 44360303

Reviewer: Masih Hashim
Study Completion Date: January 13, 1997
Study No.: 986/003

Testing Facility: Safepharm Laboratories, Ltd. & Tomen Agro, Inc.
Author: Blagden, S.M.

Quality Assurance (40 CFR §160.12): Included

Test Material: Select® Super Herbicide TM-5403
Species: Rats; Sprague-Dawley CD
Age: Approximate 8-10 weeks
Weight: Males: 275-308 g; Females: 204-223 g

Source: Charles River (UK) Ltd, Margate, Kent

Conclusion:

1. LC_{50} (mg/kg):
   Males: >5.51 mg/L
   Females: >5.51 mg/L
   Combined: >5.51 mg/L
2. The estimated LC_{50} is >5.51 mg/L
3. Tox. Category: IV

Classification: Acceptable

Procedure (Deviations from §81-3): None

Exposure Concentration mg/L (Gravimetrically Determined)	Number of Deaths/Number Tested		
	Males	Females	Combined
5.51	0/5	0/5	0/10

Clinical Observations: No animals died during the study. During the exposure, the animals had wet fur, red/brown staining around the nose/mouth, piloerection, hunched posture, noisy respiration, decreased/increased respiration rate, ptosis, and/or ataxia. One hour after the exposure, the animals showed lethargy in addition to the above signs. All rats recovered by day 4 and had normal body weight gains with the exception that one female had very slight weight loss during the first week of the study.

Gross Necropsy Findings: No abnormalities were detected.

Chamber Atmosphere		
Grav. Conc.	MMAD	GSD
5.51 mg/L	1.6 μm	0.41

Other Information: Approximately 85% of particles had an aerodynamic diameter <4 μm.

5

Chamber Environment	
Chamber Volume	30 L
Airflow	20 LPM
Temperature	19-20°C
Relative Humidity	48-56%

DATA REVIEW FOR PRIMARY EYE IRRITATION TESTING (§81-4, 870.2400)

Product Manager: 23
MRID No.: 44360304

Reviewer: Masih Hashim
Study Completion Date: December 12, 1996
Study No.: 986/005

Testing Facility: Safepharm Laboratories, Ltd. & Tomen Agro, Inc.
Author: Driscoll, R.

Quality Assurance (40 CFR §160.12): Included

Test Material: Select® Super Herbicide TM-5403
Dosage: 0.1 mL
Species: Rabbits; Albino, New Zealand White
Age: 12-16 weeks
Weight: Males and Females: 2.42-2.99 kg

Source: David Percival Ltd., Moston, Sandbach, Cheshire, UK

Conclusion:

1. Toxicity Category: IV
2. Classification: Acceptable

Procedure (Deviations from §81-4): None

Observations	Number of "positive"/number tested			
	Hours			
	1	24	48	72
	Unwashed eyes			
Corneal Opacity	1/6 [a]	0/6	0/6	0/6
Iritis	0/6	0/6	0/6	0/6
Conjunctivae:				
Redness	6/6	1/6	0/6	0/6
Chemosis	6/6	0/6	0/6	0/6
Discharge	4/6	0/6	0/6	0/6

[a] Dulling of the normal lustre of the cornea

7

DATA REVIEW FOR PRIMARY DERMAL IRRITATION TESTING (§81-5, 870.2500)

Product Manager: 23
MRID No.: 44360305

Reviewer: Masih Hashim
Study Completion Date: December 12, 1996
Study No.: 986/004

Testing Facility: Safepharm Laboratories, Ltd. & Tomen Agro, Inc.
Author: Driscoll, R.

Quality Assurance (40 CFR §160.12): Included

Test Material: Select® Super Herbicide TM-5403
Dosage: 0.5 mL
Species: Rabbits; Albino, New Zealand White
Age: 12-16 weeks
Weight: Males: 2.48-2.80 kg

Source: David Percival Ltd., Moston, Sandbach, Cheshire, UK

Conclusion:

1. Toxicity Category: III (moderate irritation; PDIS = 3.8)
2. Classification: Acceptable

Procedure (Deviations from §81-5): None

Results: One hour after patch removal, slight irritation was present at all sites characterized by well-defined erythema with very slight edema. The edema advanced to slight in 4/6 rabbits from the 24 hour observation through 72 hours and cleared by day 7. The edema on one rabbit became slight at the 48 hour observation and cleared by day 7. The edema on another rabbit continued as very slight and cleared by day 7. Well-defined erythema on one rabbit subsided to very slight by day 7 and cleared by day 14. All other rabbits had well-defined edema that cleared by day 7. Three rabbits had skin reactions that extended approximately 3 cm beyond the treatment sites; all sites cleared by day 7. Four rabbits had lost skin elasticity and flexibility by the 72 hour observation. Crust formation was found on all six rabbits at the day 7 observation. At the termination of the study, four rabbits had slight desquamation.

Special Comments: None

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (§81-6, 870.2600)

Product Manager: 23
MRID No.: 44360306

Reviewer: Masih Hashim
Study Completion Date: January 24, 1997
Study No.: 986/011

Testing Facility: Safepharm Laboratories, Ltd. & Tomen Agro, Inc.
Author: Driscoll, R.

Quality Assurance (40 CFR §160.12): Included

Test Material: Select® Super Herbicide TM-5403
Positive Control Material: 1-Chloro-2,4-dinitrobenzene (DNCB)
Species: Guinea pigs; Albino, Dunkin Hartley
Age: Approximate 8-12 weeks
Weight: Males: 397-450 g
Source: David Hall Limited, Burton-on-Trent, Staffordshire, UK
Method: Buehler

Conclusion:

1. There is no indication that this product is a dermal sensitizer.
2. Classification: Acceptable

Procedure (Deviations from §81-6): None

Procedure: For the induction phase, an unspecified amount of the undiluted test material was applied under occlusion for six hours once each week for three weeks. Guinea pigs were left untreated for two weeks before challenge. The animals were challenged with the undiluted test material and 75% v/v test material in distilled water at naive sites for 6 hours under occlusion. The naive control group was treated with undiluted test material and 75% v/v test material in distilled water at challenge only. Reactions were scored at 24 and 48 hours post exposure.

Results: Very slight erythema on 9/20 animals was elicited by the test material at the induction phase. Very slight erythema developed on 6/20 animals 24 hours following challenge with undiluted test material. Two animals showed very slight erythema 24 and 48 hours following challenge with 75% v/v test material in distilled water. Two naive control animals only had very slight erythema following challenge with undiluted test material. The historical positive control (DNCB) data (March 1995 to September 1996) were included to support the testing system. The results were appropriate.

ACUTE TOX ONE-LINERS

1. PC CODE: 121011
2. CURRENT DATE: 2-20-97
3. TEST MATERIAL: Select® Super Herbicide TM-5403

121011 Clethodim 13.2%

Study/Species/Lab Study #/Date	MRID	Results	Tox. Cat.	Core Grade
Acute oral toxicity rat/Safepharm Laboratories, Ltd. & Tomen Agro, Inc., 986/001/12-12-96	443603-01	LD_{50} > 5000 mg/kg	IV	A
Acute dermal toxicity rat/Safepharm Laboratories, Ltd. & Tomen Agro, Inc., 986/002/12-12-96	443603-02	LD_{50} > 2000 mg/kg	III	A
Acute inhalation toxicity rat/Safepharm Laboratories, Ltd. & Tomen Agro, Inc., 986/003/1-13-97	443603-03	LC_{50} > 5.51 mg/L	IV	A
Primary eye irritation rabbit/Safepharm Laboratories, Ltd. & Tomen Agro, Inc., 986/005/12-12-96	443603-04	Slight irritant; dulling of the normal lustre of the cornea in 1/6 rabbits; conjunctival irritation at 1 hour, 5/6 recovered by 24 hours, 6/6 by 48 hours	IV	A
Primary dermal irritation rabbit/Safepharm Laboratories, Ltd. & Tomen Agro, Inc., 986/004/12-12-96	443603-05	PDIS = 3.8; all rabbits had well-defined erythema and edema through 72 hours; 5/6 rabbits cleared of erythema, but all had crust formation by day 7; 4/6 rabbits had slight desquamation by day 14; all rabbits cleared of edema by day 7.	III	A
Dermal sensitization guinea pig/Safepharm Laboratories, Ltd. & Tomen Agro, Inc., 986/011/1-24-97	443603-06	Not a sensitizer	–	A

Core Grade Key: A = Acceptable