7-13-93

MEMORANDUM

59639-TI

SUBJECT: EPA Reg. No./File Symbol Select 0.94 EC
Herbicide

FROM: William S. Woodrow WSW 5-28-92
Precautionary Review Section
Registration Support Branch E 7/13/93
Registration Division (H75-05C)

TO: _____ (PM___)
Registration Division (H75-05C)

APPLICANT: Valent
Suite 600
1333 North California Blvd.
Walnut Creek, CA 94596 8025

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Clethodim	12.6
Inert Ingredient(s):	87.4
Total	100.0%

BACKGROUND

The Valent USA Corp. submitted acute dermal, acute oral and primary dermal irritation studies to support registration of Select Herbicide (Select 0.94 EC Herbicide), EPA Reg. NO. 59639-TI.

Valent stated that "This new formulation is similar to Select 2 EC Herbicide (EPA Reg. NO. 59639-3), and contains approximately half as much A.I. ingredient as Select 2 EC Herbicide". (Woodrow and Ellwanger agreed that the two Confidential Statements of Formula are substantially similar, and that therefore the Select 2 EC acute tox. data would support Select 0.94 EC (59639-TI). (The product currently considered contains 13.8% by wt. of A.I. (Clethodim Technical), whereas the Select 2 EC Herbicide (59639-3) contains 29.17% A.I. Clethodim technical.

MRID NOS. used for the new studies were 422865-02, -03, and -04.

RECOMMENDATIONS

1) The three acute toxicity studies submitted by Valent were acceptable. the acute oral and acute dermal studies were graded Core Guideline data. The dermal irritation study was graded Core Minimum Data:

a. The Primary Irritation Index score was calculated to be 4.2, whereas a re-calculation indicated the P.I. Index to be 5.11.

b. Test animal weights were not given.

2) Current acute toxicity profile for Select 0.94% EC Herbicide (59639-II):

A. Studies reviewed in present report:

study	Classification tox. Category
acute oral LD_{50} M > 5g/kg	Guideline
F = 4.8 g/kg	III
acute dermal LD_{50} > 5.0 g/kg	Guideline IV
skin irritation P.I Index = 5.11	Minimum II

Acute toxicity profile continued

B. Tests performed using the active ingredient, or: Select 2EC (Reg NO. 59639-3):

study	Classification Tox. Category
a. Technical material (code RE-45601 - Clethodim Technical)	
acute oral LD_{50} (M) - 3.61 g/kg, (F) = 2.92 g/kg. Guideline	III
acute inhalation LC_{50} > 3.9 mg/L (M&F) Minimum	III
eye irritation - Clearing irrit after 72 hrs Guideline	III
skin irritation (Technical A.I.) Minimum	II
dermal sensitization Mod. Buehler - not a sensitizer Guideline	
b. Select 2EC (59639-3)	
acute inhalation LC_{50} > 5.4 (4.4-5.8) mg/L Minimum	IV
eye irritation (select-2EC) Minimum	II

tox profile cont.

b. Select 2EC (59639-3)

study	Classification Tox. Category
dermal sensitization - not a sensitizer	—
	Minimum

4) Acute toxicity summary:

	Tox. Category
acute oral LD_{50} 4.8 g/kg	III
acute dermal LD_{50} > 5.0 g/kg	IV
acute inhalation LC_{50} > 5.4 mg/L	IV
eye irritation	II
skin irritation	II
dermal sensitization - not a sensitizer	—

LABELLING

1) Change the label signal word from DANGER to read "WARNING".

2) Change the Precautionary Statements as follows:

"Causes substantial but temporary eye injury. Causes skin irritation. Harmful if swallowed. Do not get in eyes or on clothing. Wear Goggles, face

shield or safety glasses. Wash thoroughly with soap and water after handling. Remove contaminated clothing and wash before reuse.

3) Under Statements of Practical Treatment :

Change the If on SKIN statement to read " Wash with plenty of soap and water. Get medical attention. "

ADDITIONAL RECOMMENDATION

5) No additional acute toxicity data is required for Select 0.94 EC (EPA Reg. No. 59639-TI.)

LABELING :

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

Product Manager: (23) 2-25-91 Reviewer: ~~M. Walker~~ Woodrow
MRID No.: 422865-02 Report Date: 5-26-92
Testing Facility: Chevron Env. Health Cent. Report No. CEHC 3215
Author(s): B. C. Rodgers
Species: M & F Rats, Sprague Dawley
Age: young adult M & F Observation Days (Post Exposure): (14); other ( )
Weight: M 260-287M, F206-228g.
Source: Bantin & Kingman
Test Material: Select 0.94 EC (coded SX-1850) 13.9% Select, liquid
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Conclusion:

1. LD_{50} (mg/kg): Males = > 5.0 g/kg ; Females = 4.89 g/kg. ; Combined = ____
2. The estimated LD_{50} is 4.89 g/kg.
3. Tox. Category: III. Classification: Guideline

Procedure (~~Deviations From §81-1~~): Animals acclimated (9 days prior to test, and fasted overnight before dosing. Dosed animals observed daily to death or 14 days for toxic signs/mortality ~~Body~~ Results: weights were recorded days 0, 2, 7 & 14 days. All animals subjected to gross necropsy.

Reported Mortality

DOSAGE (gr /kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5.0 g/kg	1/5	3/5	4/10
2.0 g/kg	—	0/5	0/5
7.0 g/kg	—	4/5	4/5
3.5 g/kg	—	3/5	3/5
non/dosed animals	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

Clinical: Body weight - male rats (dosed) all gained wt. Females lost wt at 5, & 7 g/kg), remaining rats gained. Salivation, diarrhea day of dosing, crusted eyes, gait, ataxia, abnormal respiratory sounds bradypnea, red ocular discharge, uro-genital discharge, hunched posture. Collapse, tremors.

Necropsy: Microscopic lesions in stomachs (5.0, 7.0 dose); multifocal to widespread necrosis of nonglandular epithelium, secondary hyperplasia of adjacent gastric epithelium.

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

Product Manager: (23) 4-24-91 Reviewer: ~~H. Walker~~ Woodrow
MRID No.: 422865-03 Report Date: 5-26-92
Testing Laboratory: Chevron Environ. Health Ctr. Report No. CEHC 3216
Author(s): B.C. Rodgers
Species: Rats, Sprague Dawley
Sex: M & F Wt.: M 325-360, F 244-286g
Test Material: Select 0.94 EC (SX-1850), liquid
Quality Assurance (40 CFR §160.12): yes (Q.A. & G.L.P.)

Summary:

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

Procedure (~~Deviations From §81-2~~): Animals were acclimated 27 days prior to dosing. Hair on backs of 5M & 5F was clipped on day before dosing. 5 g/kg applied to backs of each 5M & 5F rats. Doses covered w/ plastic film wrapped around trunk; secured with tape. A plastic collar placed on each animal.

~~Results~~: Reported Mortality

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

~~Symptomology & Gross Necropsy Findings~~:

24 hour exposure. (Wrappings removed, animals observed for 14 days for toxic signs/mortality. (daily). Animals weighed days 0, 2, 7 & 14 & day. Necropsies performed. All animals - clinical: Ocular & nasal discharge & brown anogenital staining in both treated and untreated animals of both sexes - not treatment related. Bodyweights Bodyweight loss (scattered in both sexes)

Necropsy - No gross abnormalities.

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

Product Manager: (23) 2-13-91 Reviewer: ~~N. Walker~~ (Woodrow)
MRID No.: 422865-04 Report Date: 5-26-92
Testing Laboratory: Chevron Environ. Heal. Center Report No. CEHC 3218
Author(s): B.C. Rodgers
Species: Rabbit, N.Z. White
Age: 11-13 weeks
Sex: not given
Weight: not given
Dosage: 0.5ml
Test Material: 0.94 EC Select (SX-1850) yellow liquid (13.9% A.I.)
Quality Assurance (40 CFR §160.12): yes (Q.A. + G.L.P.)

Summary:

The Primary Irritation Index = 5.11

Toxicity Category: II wts. not given.

Classification: Core Minimum (P.I. calculation was 4.2)

~~Procedure (Deviations From §81-5):~~ 6 animals acclimated for 20 days prior to test. Fur on back of 6 rabbits clipped the day before testing. 0.5ml of material applied to each of two intact sites on back of each rabbit. 1 site covered w/ gauze patch secured w/ tape.
~~Results:~~ Trunks of animals loosely wrapped with sheet of plastic film / paper towels wrapped around the plastic + secured w/ tape.
Restrainers (collars) placed on each animal. 4 hour exposure. (Wrappings removed, sites wiped w/ moistened pads. Irritation scored at 1, 24, 48, 72 hours after test material removed + at 7 + 14 days, according to the Draize method.

	time	mean scores: erythema	edema
1) scores for ER-EC added for each animal (for 24, 48 + 72 hours), ÷ 3 = mean of the resulting 6 scores = P.I. = 5.11	1 hr	1.6	1.2
	24 hrs	2.2	1.4
	48 hrs	3.0	2.4
	72 hrs	3.7	2.6
	7 days	4.0	1.7
	14 days	0.3	0.0

~~Special Comments:~~

P.I. Index for
select 0.94 EC
Herbicide
59639-TI

1

dermal irritation

24 hrs	3	3	2	2	2	2
	+2	+3	+1	+1	+1	+1
	5	6	3	3	3	3
48	3	4	3	3	2	3
	+2	+4	+2	+3	+2	+2
	5	8	5	6	4	5
72	4	4	4	4	2	4
	+2	+4	+2	+3	+2	+3
	6	8	6	7	4	7
	16	22	14	16	11	15
	5.3	7.3	4.6	5.3	3.6	5

3

Mean = 5.11 = P.I.

Tox Chem. No. 721 F

File Last Updated

Current date 5-26-92

Study/Species/Lab/Study# Date	Material	MRID No.	Results	Tox. Cat.	Core Grade
acute oral LD50, Rat Chevron Environ Health Center # CEHC 3215 2-25-91	Select 0.94 EC	422865 -02	LD50 > M > 5.0 g/kg. F = 4.8 g/kg	III	Guide-line
acute dermal LD50, Rat Chevron Environ. Health Cent. # CEHC 3216 4-24-91	"	422865 -03	LD50 > 5.0 g/kg	IV	Guide-line
skin irritation, Rabbit Chevron Environ. Health cent. # CEHC 3218 2-13-91	"	422865 -04	P.I. Index = 5.11	II	mini-mum