(3-2-89)

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

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg. No./File Symbol 352-LEG
DuPont Avatar Herbicide (20DF Formulation)

FROM: William S. Woodrow WSW 2-28-89
Precautionary Review Section
Registration Support Branch
Registration Division (TS-767C)
E 3/2/89
DAS 3/2/89

TO: Robert J. Taylor (PM 25)
Fungicide-Herbicide Branch
Registration Division (TS-767C)

APPLICANT: DuPont
Walker's Mill, Barley Mill Plaza
Wilmington, Delaware 19898

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
Chlorsulfuron: [2-chloro-N-[(4-methoxy-6-methyl)-1,3,5-triazin-2-yl)-aminocarbonyl]benzene-sulfonamide	15 %
Metsulfuron Methyl: (Methyl 2-[[[[4-Methoxy-6-methoxy-[3,5-triazin-2-yl]-amino]carbonyl]-amino]sulfonyl] benzoate	5 %
Inert Ingredient(s):	80.0%
Total	100.0%

1/10

BACKGROUND:

DuPont submitted Acute otal, Acute dermal, Primary eye and Primary dermal irritation, and sensitization studies in support of DuPont Avatar Herbicide (20DF Formulation) for Registration. MRID NO.'s included 406227-01 through 406227-05.

RECOMMENDATION:

1) The Acute otal, Acute dermal, Primary eye and Primary dermal irritation, and the Dermal sensitization toxicity studies submitted are acceptable to Registration Support Branch/ PRS ~~LABELING~~.

2) The Primary eye irritation study was graded "Core Minimum Data", due to lack of re-grinding the product powder used, to ensure a very fine product for animal testing.

3) It will be necessary to submit an acceptable Acute inhalation toxicity study, using DuPont Avatar Herbicide product intended for commerce, further ground with laboratory equipment. Dusts which contain primarily large particles also contain small amounts of fine particles derived, in part, from the manufacturing

As discussed with PM, This is in conflict with the regulations. Therefore no inhalation study is required at the time.

process, or by the rubbing action between the particles during transport. Thus, all dusts and sprays regardless of the anticipated aerosol sizes are to be tested.

LABELING:

1) The product Hazard signal word "CAUTION" is acceptable.

2) Under Precautionary Statements Change "In case of contact with eyes" to read, "In case of contact with eyes or skin,"

3) Precautionary labeling may require further revision upon submission of outstanding studies.

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

Product Manager: (25) Reviewer: ~~M Waller~~ Woodrow
MRID No.: 406227-01 Report Date: 2-27-89
Testing Facility: Dupont Haskell Lab. Report No. 113-88
Author(s): Calvin N. Wylie
Species: Rat, 5M x 5F
Age: 7 wk old Observation Days (Post Exposure): (14); other ( )
Weight: M206-223, F177-194
Source: Charles River Breeding Labs.
Test Material: Benzene sulfonamide (INH-9637-4) 20% pure
Quality Assurance (40 CFR §160.12): Satisfactory

Conclusion:

1. LD_{50} (mg/kg): Males = > 5000 mg/kg; Females = same; Combined = —
2. The estimated LD_{50} is > 5000 mg/kg
3. Tox. Category: IV. Classification: Core Guidelines

Procedure ~~(Deviations From §81-1)~~: 5000 mg/kg in Corn oil administered by intubation. Body weights. Observations to 14 days & gross necropsy (3 males & 3 females).

Results: no mortality

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
5000 mg/kg	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

The only clinical signs shown that females exhibited a slight weight loss.
No abnormalities were revealed during gross necropsies.

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

Product Manager: (25) — Reviewer: ~~M. Waller~~ Woodrow
MRID No.: 406227-02 — Report Date: 2-27-89
Testing Laboratory: Hazleton Labs. — Report No. 201-811
Author(s): James L. Garsus
Species: Rabbit; N.Z. White
Sex: 5M & 5F — Wt.: M2342-2772, F2575-2759
Test Material: Benzenesulfonamide (INH-9637-4) 20% pure (powder)
Quality Assurance (40 CFR §160.12): Satisfactory

Summary:

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

Procedure ~~(Deviations From §81-2):~~ All shaved Dorsal area shaved, abraded, treated with 2000 mg/kg test material, held in contact for 24 hrs. using nonabsorbent bandage + 24 hrs contact, sites wiped, observed for mortality, signs of toxicity 1X Daily for 14 Days + necropsies. Body weights.

Results:

Reported Mortality

DOSAGE (mg/kg)	(NUMBER KILLED/NUMBER TESTED) Males	Females	Combined
2000 mg/kg	0/5	0/5	0/10

Symptomology & Gross Necropsy Findings:

One animal lost weight at termination, remainder had gained weight by Termination. The only abnormal sign of toxicity was anorexia for animal Days 3+4, one animal on Day 5. No erythema, edema or other effects.

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

Product Manager: (25)
MRID No.: 406227-03
Testing Laboratory: Hazleton Labs.
Author(s): James L. Garcas
Species: Rabbit, N.Z. white
Sex: M-A. Weight: M.A.
Source: Hazleton Dutchland
Dosage: 54 mg/eye
Test Material: Benzene sulfonilamide 20 g pure off-white powder
Quality Assurance (40 CFR §160.12): Satisfactory

Reviewer: ~~M. Waller~~ Woodrow
Report Date: 2-27-89
Report No. 201-83

Summary:
1) should have ground powder as fine as possible
2) should have calculated P.I. Index

Tox. Category: IV Classification: Core Minimum

Procedure (~~Deviation from §81-4~~): 54 mg aliquot placed into conjunctival left eye sac of 9 rabbit eyes (9 rabbits). Treated eye of 3 rabbits washed for 1 min, 10 sec. after treatment. Irritation scored according to Draize at 24, 48 & 72 hrs

Results:

	Observations (number "positive"/number tested)							
	Hour	Days						
	1	1	2	3	4	7	14	21
Cornea Opacity		0/9	0/9	0/9				
Iris		0/9	0/9	0/9				
Conjunctivae Redness		2/9	0/9	0/9				
Chemosis		4/9	0/9	0/9				
Discharge		0/9	0/9	0/9				

Comments: No corneal opacity, iritis, chemosis in unwashed eyes. The tester should have ground powder to a state as fine as possible, using laboratory equipment. The P.I. Index should have been calculated

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

Product Manager: (25)
MRID No.: 406227-04
Testing Laboratory: Hazleton Labs.
Author(s): James L. Gargus
Species: Rabbit, NZ white
Age: young adult
Sex: males
Weight: N.A.
Dosage: 0.5ml
Test Material: Benzenesulfonamide 20% pure offwhite powder
Quality Assurance (40 CFR §160.12): Satisfactory

Reviewer: ~~M. Weller~~ Woodrow
Report Date: 2-27-89
Report No. 201-812

Summary:

The Primary Irritation Index = 0 to 1.0

Toxicity Category: III

Classification: Core Guidelines

Procedure (~~Deviations From §81-5~~): 0.5ml aliquot test material under 1" Sq. gauze, tape & damming; 24 hr contact. Dermal responses scored at 24, 48, 72hrs, days 4, and 7. 4 test sites/rabbit; 2 abraded & 2 intact.

Results:

5/6 rabbits showed no irritation of any kind. One rabbit showed mild erythema, at both abraded and intact skin sites, at 24, 48 and 72 hours. No further irritation was shown by this rabbit (at 4 or 7 days; with the exception of mild erythema at both abraded sites at 4 days. The P.I. score (undiluted) ranged from 0 to 1.0.

Special Comments:

DuPont Avatar Herbicide may be considered a moderate skin irritant (moderate irritation at 72 hours (moderate erythema).

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

Product Manager: (25)
MRID No.: 406227-05
Testing Laboratory: Hazleton Labs.
Author(s): James L. Garvis
Species: Hartley Guinea Pigs
Sex: 23 M Weight: N.A.
Source: Hazleton Dutchland, Inc.
Test Material: Benzene sulfonamide (DuPont Avatar, 20DF, 20% pure.)
Positive Control Material: none
Quality Assurance (40 CFR §160.12): satisfactory

Reviewer: Woodrow ~~M. Waller~~
Report Date: 2-28-89
Report No. 201-814

Method: Modified Buehler Test

Summary:
1. This product is / (is not a dermal sensitizer)
2. Classification: Core Guidelines data.

Procedure ~~(Deviation From §81-6)~~: Primary Irritation - 10 g.p. received, separately, 5% or 50% suspensions of test material in saline in 0.05 ml aliquots at separate sites. 10 control animals received 0.05 ml aliquots of saline only. Irritation ~~Results~~: scores of test animals were compared to challenge scores at end of sensitization period.

Intradermal injection - same 20 animals were treated in the injection phase. 0.1 ml aliquot of the test material suspension (1% in saline) was given to test animals (10) following the last primary irritation reading. Control animals (10) were intradermally injected with 0.1 ml of saline.

The injections (both test and control) were repeated on alternate sides of the sacral/hip area weekly for 3 additional weeks, to total 4 injections.

Challenge - 13 days after last injection treatment, all animal backs were shaved. 0.05 ml aliquots of a 5% and a 50% suspension was applied to the 2 previously used test animal sites, and also applied to each of the 10 control

animals - 24 & 48 hours after induction, challenge, primary irritating, and challenge phases skin sites were examined and scored according to Draize - After induction treatments, test sites were observed for necrosis and erythema at 24 hours only. All animals observed for illness and mortality.

Results - No mortality.

1) Primary irritation and Sensitization (Induction) topical applications

a) Test animals (each animal received 5% or 50% injections) 1 (of 10) at 50% showed mild erythema

(b) Control - all 10 animals negative

2) Test animals: Intradermal injections

(a) week 1 - 6 animals - mild erythema (0.1 ml of 1.0% in saline)

(b) week 2 - 5 animals - mild erythema "

(c) week 3 - 6 animals - mild erythema "

(d) week 4 - 2 animals - mild erythema "

(e) Control animals (10) - all negative for erythema & edema

3) Challenge(s)

(a) Test animals (13 days after last induction) 0.05 ml of 5% or 50% test suspension - applied topically at same test sites as for induction - all negative results.

b) Controls - All negative results.

AVATAR 20%
194AA (2-chlorsulfuton)

Tox Chem No. 419H (metsulfuton) File Last Updated _____ Current Date 2-28-89

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD_{50}, LC_{50}, PIS, NOEL, LEL	TOX. Cat.	COI Doc
Acute oral tox, Rat DuPont Haskell lab. # 113-85. 3-20-85	20% Benzene sulfonamide 2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl) amino carbonyl]-, c methyl-2[[[[(4 methoxy-6-methyl-1,3,5-triazin-2-yl)amino] carbonyl]amino sulfonyl] benzoate	406227 -01	LD_{50} > 5000 mg/kg	IV	Guid line
Acute dermal tox., Rabbit Hazleton Labs. # 201-811. 4-25-85	"	406227 -02	LD_{50} > 2000 mg/kg.	III	Guid line
Primary eye irritation, Rabbit. Hazleton labs. #201-83. 4-23-85	"	406227 -03	2/9 showed mild erythema } 24 hrs 4/9 " mild chemosis } No other adverse effects (should have cleared by 72 hrs)	IV	min- imum
Primary dermal irritation, Rabbit: Hazleton, Labs. # 201-812. 4-25-85	"	406227 -04	DuPont Avatar 20% may be considered a moderate skin irritant.	III	Guid lines
Dermal Sensitization, Guinea Pig Hazleton Labs. # 201-814. 4-29-85	"	406227 -05	DuPont Avatar 20% was not a skin sensitizing agent	—	Guid line

(10)