

(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
Du Pont Avatat 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
RS 3/2/89

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

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

FORMULATION FROM LABEL:

Active Ingredient(s):	% by wt.
<u>Chlorosulfuron: 1,2-chloro-N-[(4-methoxy-6-methyl)-</u>	
<u>-1,3,5-triazin-2-yl]-aminocarbonyl] benzene-</u>	
<u>sulfonamide</u>	<u>15.9%</u>
<u>Metsulfuron Methyl: (Methyl 2-[[[4-methoxy-6-methoxy-</u>	
<u>-1,3,5-triazin-2-yl]-amino] carbonyl]-amino] sulfonyl]</u>	<u>5%</u>
Inert Ingredient(s):	<u>80.0%</u>
benzoate Total	100.0%

1/10

BACKGROUND:

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

RECOMMENDATION:

1) The Acute oral, Acute dermal, Primary eye and Primary dermal irritation, and the Dermal sensitization toxicity studies submitted are acceptable to Registration Support Branch/

~~PRR~~
~~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 P.M., 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
 MRID No.: 406227-01 Report Date: 2-27-89
 Testing Facility: DuPont Haskell Lab. Report No. 113-85
 Author(s): Calvin N. Wylie
 Species: Rat, 5M x 5F
 Age: 7 wk old Observation Days (Post
 Weight: M 206-223, F 177-194 Exposure): (14); other ()
 Source: Charles River Breeding Lab.
 Test Material: Benzene sulfonamide (INH-9637-4) 20% put
 Quality Assurance (40 CFR §160.12): Satisfactory

Conclusion:

1. LD₅₀ (mg/kg): Males = > 5000 mg/kg; Females = same; Combined = same
2. The estimated LD₅₀ 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
<u>5000 mg/kg</u>	<u>0/5</u>	<u>0/5</u>	<u>0/10</u>

Symptomology & Gross Necropsy Findings:

The only clinical signs showed 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: ^{Woodrow} Mr. Waller

MRID No.: 406227-02

Report Date: 2-27-89

Testing Laboratory: Hazleton Labs.

Report No. 201-811

Author(s): James L. Gargus

Species: Rabbit, New Zealand White

Sex: 5M & 5F

Wt.: M 2342-2772, F 2575-2759

Test Material: Benzene sulfonamide (INH-9637-4) 20% pure (powder)

Quality Assurance (40 CFR §160.12): Satisfactory

Summary:

- LD50 (mg/kg): Males = $> 2000 \text{ mg/kg}$; Females = $> 2000 \text{ mg/kg}$; Combined = $> 2000 \text{ mg/kg}$
- The estimated LD50 is $> 2000 \text{ mg/kg}$
- Tox. Category: III. Classification: Core Guidelines

Procedure (~~Deviations From §81-2~~): All shaved dorsal areas shaved, abraded, treated with 2000 mg/kg test material, held in contact for 24 hrs. seeing nonabsorbant bandage. 24 hrs contact, sites wiped, observed for mortality, signs of toxicity 1x daily to 14 days. 2 necropsies.

Results: Body weights.

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 by animal days 3 & 4, and one animal on day 5. No erythema, edema or other effects.

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

Product Manager: (25) Reviewer: Woodrow M. Waller
 MRID No.: 406227-03 Report Date: 2-27-89
 Testing Laboratory: Hazleton Labs. Report No. 201-83
 Author(s): James L. Gargues
 Species: Rabbit, N.Z. white
 Sex: N.A. Weight: N.A.
 Source: Hazleton Dutchland
 Dosage: 54 mg/eye
 Test Material: Benzene sulfonamide 20% pure off-white powder
 Quality Assurance (40 CFR §160.12): Satisfactory

Summary:

- 1) should have ground powder as fine as possible
- 2) should have calculated P.T. Index

Tox. Category: IV Classification: Core Minimum

Procedure (Deviation from §81-4): 54 mg aliquot placed into conjunctival
left eye sac of 9 rabbits (9 rabbits). Treated eye of 3 rabbits washed
for 1 min, 10 sec. after treatment. Irritation scored according to
Oraing 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 immediate days
The tester should have re-ground powder to a state
as fine as possible, using laboratory equipment.
The P.T. Index should have been calculated

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

Product Manager: (25)

MRID No.: 406227-04

Testing Laboratory: Hazelton Labs.

Author(s): James L. Gargas

Species: Rabbit, NZ white

Age: young adult

Sex: males

Weight: N.A.

Dosage: 0.5ml

Test Material: Benzene sulfonamide 20% pure off white powder

Quality Assurance (40 CFR §160.12): Satisfactory

Reviewer: L. Woodrow M. Waller
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 & bandaging; 24 hr contact. Dermal responses scored at 24, 48, 72 hrs, 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 (individual) ranged from 0 to 1.0.

Special Comments:

Dee Pont 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)

Reviewer: Woodrow M. Waller

MRID No.: 406227-05

Report Date: 2-28-89

Testing Laboratory: Hazleton Labs.

Report No. 201-814

Author(s): James L. Gargus

Species: Hartley Guinea Pigs

Sex: 23 m

Weight: N.A.

Source: Hazleton Dutchland, Inc.

Test Material: Benzene sulfonamide (DuPont Avatex, 20 DF, 20% pure.)

Positive Control Material: none

Quality Assurance (40 CFR §160.12): satisfactory

Method: Modified Buehler Test

Summary:

1. This product is / is not a dermal sensitizer.
2. Classification: Carc. 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 induction - same 20 animals were treated in the induction phase. 0.1 ml aliquot of the test material suspension (1% in saline) was given to test animals 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 induction 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

2.

animals - 24 & 48 hours after - range finding, primary irritating, and challenge phase skin sites were examined and scored according to Dring. 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 2090

1944AA (2-chlorosulfuton)

Tox Chem No. 419A

File Last Updated

Current Date 2-28-89

Study/Lab/Study #/Date	Material	EPA Accession No.	Results: LD50, LC50, PIS, NOEL, LEL	TOX. COI Cat. Doc
Acute oral tox, Rat DuPont Haskell Labs. # 113-85-3-20-85	20% Benzene sulfonamide 2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino carbonyl], 2-methyl-2-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino] carbonyl]amino sulfonyl] benzoate	406227-01	LD50 > 5000mg/kg	IV Guideline
Acute dermal tox. Rabbit Hazleton Labs. # 201-811. 4-25-85	"	406227-02	LD50 > 2000 mg/kg	III Guideline
Primary eye irritation, Rabbit Hazleton Labs. # 201-83-4-23-85	"	406227-03	2/9 showed mild conjunctivitis 4/9 " mild chemosis NO other adverse effects (should have been stained powder)	IV minimum
Primary dermal irritation, Rabbit Hazleton Labs. # 201-812-4-25-85	"	406227-04	DuPont Avatac 20% may be considered a moderate skin irritant.	III Guideline
Dermal Sensitization, Guinea Pig Hazleton Labs. # 201-814-4-29-85	"	406227-05	DuPont Avatac 20% was not a skin sensitizing agent	- Guideline