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)

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):

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>% by wt.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorosulfuron</td>
<td></td>
</tr>
<tr>
<td>1,2,5-Triazin-3-yl</td>
<td></td>
</tr>
<tr>
<td>4-Methoxy-6-Methyl</td>
<td></td>
</tr>
<tr>
<td>1,3,5-Triazin-2-yl</td>
<td>15.9%</td>
</tr>
<tr>
<td>4,6-Dimethoxysulfonamide</td>
<td></td>
</tr>
<tr>
<td>Inert Ingredient(s):</td>
<td>80.8%</td>
</tr>
</tbody>
</table>

Total 100.0%
BACKGROUND:

Du Pont submitted Acute oral, Acute dermal, Primary eye and Primary dermal irritation, and sensitization studies in support of Du Pont Avatar Herbicide (2005 Formulation) for Registration. MRID No.'s included 406277-01 through 406277-05.

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.

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 Du Pont 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. Walter
MRID No.: 406-227-01 Report Date: 2-27-89
Testing Facility: Oakport Haskell Lab. Report No. 113-89
Author(s): Calvin N. Wylie
Species: Rat ; M 15 M 5 F
Age: 7 wk old Observation Days (Post Exposure): (14) other ( )
Weight: M 206-223, F 177-194
Source: Charles River Breeding Labs.
Test Material: Benzene sulfonamide (INH-96-37-4) 20% pure
Quality Assurance (40 CFR §160.12): Satisfactory

Conclusion:

1. LD50 (mg/kg): Males = >5000 mg/kg ; Females = same ; Combined =
2. The estimated LD50 is >5000 mg/kg

Procedure (Deviations From §81-1): 5000 mg/kg in corn oil administered by intubation. Body weight, Observation to 14 days, gross necropsy (3 males + 3 females).

Results: No mortality

<table>
<thead>
<tr>
<th>DOSAGE (mg/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Males</td>
</tr>
<tr>
<td>5000 mg/kg</td>
<td>0/5</td>
</tr>
</tbody>
</table>

Symptomology & Gross Necropsy Findings:
The only clinical signs showed that females exhibited a slight weight loss.
No abnormalities were revealed during gross necropsy.
DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (§81-2)

Product Manager: (25) 
MRID No.: 406227-02 
Testing Laboratory: Hazleton Labs. 
Author(s): James L. Cargus 
Species: Rabbit, Male White 
Sex: MALE 
Wt.: M 2742-2772, F 2578-2754 
Test Material: Benzene sulphonamide (144-9637-4) 20.7% pure/powder 
Quality Assurance (40 CFR §160.12): Satisfactory

Summary:

1. LD50 (mg/kg): Males = > 2000 mg/kg; Females = 
   Combined = 
2. The estimated LD50 is > 2000 mg/kg
3. Tox. Category: 1
   Classification: 
   Core Guidelines

Procedure (Deviation from §81-2): All animals were shaved ahead of treatment with 2000 mg/kg test material, held in contact for 24 hrs. using non-alcohol. Smaller - 24 hrs contact site wiped, dressed for mortality, signs of toxicity 1x daily to 14 days + necropsy

Results:

<table>
<thead>
<tr>
<th>DOSAGE (mg/kg)</th>
<th>(NUMBER KILLED/NUMBER TESTED)</th>
<th>Males</th>
<th>Females</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000 mg/kg</td>
<td></td>
<td>0/5</td>
<td>0/5</td>
<td>0/10</td>
</tr>
</tbody>
</table>

Symptomology & Gross Necropsy Findings:

One animal lost weight at termination, remainder had gained weight by termination. The only abnormal sign was anorexia by remainder days 3-4, and one animal on day 5. No other signs, lesions, 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. Garcia

Species: Rattus, N. T. White  
Sex: M. A.  
Weight: M. A.  
Source: Hazleton Outbred

Dosage: 5 mg/eye  
Test Material: Benzene sulphonamide 20%aqueous off-white powder

Quality Assurance (40 CFR §160.12): Satisfactory

Summary:
1) A slight hazy, cloudy appearance was noted in the cornea of both eyes of the test animal. There was slight conjunctival injection observed on the second day of observation.
2) A slight depression of the nasal bridge and slight irritation of the skin of the nose was noted.

Tox. Category: IV  
Classification: Core Minimum

Procedure (Deviation from §81-4): Crying elicited prior to conjunctival irritation or exposure. A small amount of aqueous sodium carbonate was administered to the eye of each animal immediately after the test material was applied. The animal was observed for 10 seconds after the application of the test material. Irritability was scored according to the criteria described in §81-4.

Results:

<table>
<thead>
<tr>
<th>Observations</th>
<th>(number &quot;positive&quot;/number tested)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hour</td>
</tr>
<tr>
<td>Cornea</td>
<td>1</td>
</tr>
<tr>
<td>Opacity</td>
<td>⬑/9</td>
</tr>
<tr>
<td>Iris</td>
<td>⬑/9</td>
</tr>
<tr>
<td>Conjunctivae</td>
<td></td>
</tr>
<tr>
<td>Redness</td>
<td>⬑/9</td>
</tr>
<tr>
<td>Chemosis</td>
<td>⬑/9</td>
</tr>
<tr>
<td>Discharge</td>
<td>⬑/9</td>
</tr>
</tbody>
</table>

Comments: No corneal opacities, chemosis in some subjects. The test should have been repeated with the same preparation as soon as possible, using laboratory equipment. The P.I. should have been calculated.
DATA REVIEW FOR SKIN IRRITATION TESTING (§81-5)

Product Manager: (25)  
MRID No.: 40627-04  
Reviewer: M. Walter  
Testing Laboratory: Hazleton Labs  
Report Date: 2-27-89  
Author(s): James L. Garbus  
Report No. 201-81-2  
Species: Rabbit, NZ white

Age: young adult  
Sex: male  
Weight: N.A.  
Dosage: 0.5ml  
Test Material: Benzene sulfonamide 20% pure off-white powder  
Quality Assurance (40 CFR §160.12): Satisfactory

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" syringe, tape & demersal 24hr contact. Dermal response scored at 24, 48, 72hrs. Dose 4, 0.07, 4 test sites/rabbit; 2 checked 1 intact.

Results:

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

Special Comments:

Du 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)  
MRID No.: 406227-03  
Testing Laboratory: Hazelton Labs.  
Author(s): James L. Garay  
Species: Hartley Guinea Pigs  
Sex: 23 M  
Weight: N.A.  
Source: Hazelton Dutchland, Inc.  
Test Material: Benzene sulphonamide (Du Pont Avatar, 20 DE, 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: Care 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 (1:1 in saline) was given to test  
animals following the last priming 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 scapula/hip area weekly for  
3 additional weeks, to total 5 injections.  
Challenge: 14 days after last induction treatment, all animal  
backs were shaved. 0.05 ml aliquots of 0.5% and 0.50%  
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 - rage, feeling, primary irritation, and lesions. Place skin sites were examined and scored according to Oring. After induction treatments, test sites were observed for necrosis and oogtome at 48 hours only. All animals observed for illness and mortality.

Result - No mortality.

1) Priming irritation - and deisatization (Induction) topical applications
   a) Test animals (each animal received 5% or 50% injection)
      i) 10 at 50% showed mild erythema
   b) Control - all animals negative

2) Test animals - Intradermal injections
   a) Week 1 - animals - mild erythema (0.1 ml of 10% in saline)
   b) Week 2 - 5 animals - mild erythema
   c) Week 3 - 6 animals - mild erythema
   d) Week 4 - 2 animals - mild erythema

3) Control animals (10) all negative for erythema

3) Challenge(a)
   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.
<table>
<thead>
<tr>
<th>Study/Lab/Study #/Date</th>
<th>Material</th>
<th>EPA Accession No.</th>
<th>Results:</th>
<th>TOX, COI Cat, Doc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute oral tox, Rat, Du Pont</td>
<td>20% Benzene sulfonamide 2-chloro-N-[[4-methoxy-6-methyl-1,3,5-triazin-2-yl] amino carbonyl][3’-methyl-2[[[4-methoxy-6-methyl-1,3,5-triazin-2-yl] amino] carbonyl]amino sulfonyl]3 methoxybenzylamide</td>
<td>406227-01</td>
<td>LD50 &gt; 5000 mg/kg</td>
<td>11 Guideline Line</td>
</tr>
<tr>
<td>Acute dermal tox, Rabbit, Hazleton Labs</td>
<td></td>
<td>406227-02</td>
<td>LD50 &gt; 2000 mg/kg</td>
<td>01 Guideline Line</td>
</tr>
<tr>
<td>Primary eye irritation, Rabbit, Hazleton, Labs</td>
<td></td>
<td>406227-03</td>
<td>LD50 &gt; 2000 mg/kg</td>
<td>11 Guideline Line</td>
</tr>
<tr>
<td>Primary dermal irritation, Rabbit, Hazleton, Labs</td>
<td></td>
<td>406227-04</td>
<td>LD50 &gt; 2000 mg/kg</td>
<td>11 Guideline Line</td>
</tr>
<tr>
<td>Dermal sensitization, Guinea Pig, Hazleton, Labs</td>
<td></td>
<td>406227-05</td>
<td>LD50 &gt; 2000 mg/kg</td>
<td>11 Guideline Line</td>
</tr>
</tbody>
</table>

Note: The results indicate that the substance is highly toxic, with LD50 values exceeding 2000 mg/kg for both dermal and oral exposure routes. Additional studies suggest mild eye irritation and skin irritation, with no noted adverse effects.