CASWELL FILE

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

MEMORANDUM

DATE: SEP 25 1981

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Pesticide Use Classification of Fonofos (Dyfonate) 20G
Pesticide Use Restrictions 44F. 45218 ID Notification
OPP-30029-Letter of May 4,1981
Addendum to October 26, 1979, October 23, 1980 and
February 17, 1981 Acute Toxicity Data Submitted by Stauffer
CASWELL 454B

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Conclusions

1. Dyfonate technical 95.4% (study T-6461) is in toxicity category I by the acute oral and dermal route of exposure and negative for eye and skin irritation.

2. To permit testing of this material for skin and eye irritation, the dosage levels administered were reduced one tenth of the required dose in both studies. The systemic dermal toxicity (Slope 3.93) for Dyfonate technical is of greater significance than the irritation potential of this material.

3. Stauffer has submitted corrections for the rabbit oral toxicity study on Dyfonate 20 granular (study T-6384) to clarify the relationship between the LD_{50} value reported for the 20 granular formulation and the same study used to calculate LD_{50} expressed in terms of the active ingredient.

4. The acute rat oral toxicity study in T-6461 was originally determined to be core supplemental. Stauffer has submitted additional data to upgrade the acute rat oral toxicity study from supplemental to core guideline.

Background Information

With my memo of December 20, 1979, all of the acute rat and rabbit oral toxicity studies submitted October 26, 1979 by Stauffer, reported in Appendex 3B for either the technical or 20% granular formulations were deficient in that the data was not adequate to determine the toxicity category.

With my memo of February 5, 1981 the same deficiencies were cited in the data submitted by Stauffer October 23, 1980 in the rat and rabbit studies for either the technical or 20% granular in that the animals were observed for seven days rather than the required 14 day observation period.

February 17, 1981 Stauffer submitted data fulfilling the data requirements for Staufffer study identified as T-6883 and all studies in T-6384 except those where 20% granular was reported as the calculated active ingredient. In my memo of April 29, 1981 the observations of toxicity, the rationale for terminating the following studies at seven days and gross necropsy observations were requested for the following studies:

1. Acute rat oral toxicity study T-6461 on the technical material.

2. Acute rabbit oral toxicity study T-6384 Dyfonate 20 granular calculated as the active ingredient.

Current Considerations

Stauffer in their letter of May 4, 1981 clarified the deficiencies of T-6384 and submitted a complete copy of T-6461 which included the following studies on technical (95.4%) Dyfonate.

1. Acute oral LD_{50} for male and female rats.

2. Acute dermal LD_{50} for rabbits.

3. Skin and eye irritation studies.

1. The following corrections are to be made for those studies identified as T-6384, 20% granular calculated as the active ingredient in Stauffer submission of October 26, 1979 Accession Number 243640 and submission of October 23, 1980 Accession Number 243582.

   Corrections for T-6384

   Data on pages C-1 and D-1 of T-6384 were obtained from the same test group. Data on pages C-5 and D-2 of T-6384 were obtained from the same test group. The results presented on pages C-1 and C-5 were calculated on the basis of granular DYFONATE 20-G and the results presented on pages D-1 and D-2 were calculated on the basis of active ingredients. Also page D-2 indicates the sex of the animals tested was female, when in fact the animals were male.

2. Technical Dyfonate 95.4%
   Acute Male Rat Oral Toxicity
   Stauffer Chemical Co. Report T-6461 Feb. 12, 1979. Acc. 245491

   A. Procedure

   Sixty male Sprague-Dawley albino rats weighing between 160-224 grams were divided into six groups of 10 animals per group. Animals were fasted over night. The technical material (95.4%) was administered at dosage levels of 39.9, 35.6, 31.7, 25.2, 20.0 and 14.1 mg/kg at a constant volume of 10 ml/kg in corn oil. All animals were observed for 14 days. Necropsies were performed on all animals dying during the test and on those surviving the 14 day observation period.

   B. Results

   1. LD_{50} 24.5 mg/kg (21.4-28.0)
      Slope = 1.30

   2. Pharmacotoxic Signs
      At the LD_{50} dosage level depression, tremors, copious salivation, diarrhea, bulging eyes, lacrimation, labored breathing and wet yellow stains around the ano-genital region were observed. These symptoms returning to normal by day six. Deaths at this level occured within six hours.

   3. Necropsy
      No apparent gross abnormalities were reported at the LD_{50} level.

C. Conclusion

1. Classification of Data - From Supplementary to Core Guideline.

2. Toxicity Category: I

Technical Dyfonate 95.4%
Acute Female Rat Oral Toxicity
Stauffer Chemical Co. Report T-6461 Feb. 12, 1979. Acc. 245491

A. Procedure

Eighty female Sprague-Dawley albino rats were divided into seven groups of 10 animals per group and dosed at 20, 15.8, 12.6, 11.2, 10.6 mg/kg and 15 animals per group were dosed at 10.0 and 7.9 mg/kg. Animals were fasted overnight. The technical material (95.4%) was given by intubation at a constant volume of 10 ml/kg in corn oil. All animals were observed for 14 days. Necropsies were performed on all animals dying during the study and those surviving the 14 day observation period.

B. Results

1. LD_{50} 10.8 mg/kg (9.6-12.2)
   Slope = 1.40

2. Pharmacotoxic Signs
   At the LD_{50} dosage level depression, tremors, shallow breathing, blood-like stains around the facial area and yellow stains around the ano-genital region were observed. These symptoms returning to normal by day four. Deaths at this dosage level occured within 22 hours.

3. Necropsy
   Red and irritated stomachs were reported for the animals dying during the study at the LD_{50} level (10.6 mg/kg level). At the next lower level dark livers and lungs, apparent hemorrhage in stomach and a blood like fluid in the intestine was reported of those rats dying during the test.

C. Conclusion

1. Classification of Data: From supplementary to Core Guideline.

2. Toxicity Category: I

Technical Dyfonate 95.4%
Acute Rabbit Dermal Toxicity
Staufer Chemical Co. Report T-6461 Feb. 12, 1979. Acc. 245291

A. Procedure

Four dosage levels of three male and three female New Zealand white albino rabbits weighing between 1.64 to 2.278 kg were dosed at 10,30,100 and 200 mg/kg. Two additional levels of 282 and 399 mg/kg consisted of 4 male and 4 female rabbits. The test material, 95.4% technical Dyfonate was applied to the closely clipped abdominal skin beneath a protective binder. The skin was abraded on half of the animals on each level. After a 24 hour exposure, the binder was removed, the skin was inspected for irritation, and the test site was washed with soap and water and rewrapped in a gauze binder. After three days the gauze binder was removed. All test animals were observed for 14 days following exposure. Necropsy was performed on animals dying during the 14 day observation period and those surviving the observation period.

B. Results

1. LD_{50} 159 mg/kg (40-615) male and female combined
   Slope = 3.93

2. Pharmacotoxic signs observed at the 200 mg/kg level include depression, tremors, salivation, diarrhea, rapid breathing and constricted pupils. These symptoms returned to normal by day 4. At this level there were 3/6 deaths all occurring within 5 hours. No apparent irritation was observed.

3. Necropsy of those animals dying within five hours after dosing showed red and irritated stomachs, darkened lungs and pale liver.

C. Conclusion

1. Classification of Data: From supplemental to Minimum.

   a. Deficiency - The test results are not consistent with the test procedure described in Appendex II Section B of this report, which calls for four male and four female rabbits to be used for each dosage level for the determination of an LD_{50} for each sex.

   b. This study has been upgraded from supplemental to minimum with the following considerations.

      i) There is no difference between sexes demonstrated in the rabbit oral LD_{50} values.

      ii) The rabbit dermal and eye irritation studies were conducted at dosage levels consistant with the dermal toxicity study and have been considered supplemental to this study for the number of animals tested.

Technical Dyfonate 95.4%
Skin Irritation - Rabbit
Stauffer Chemical Co. Report T-6461 Feb. 12, 1979. Acc. 245491

A. Procedure

The test material (0.05 ml) was applied undiluted to both the abraded and intact skin of six New Zealand albino rabbits. The test material was placed under a one-inch square gauze patch and secured in place with rubberized daming for 24 hours. After 24 hours patch was removed, reaction scored and the site washed. Irritation was scored according to Draize at 24, 48 and 72 hours.

B. Results

1. No irritation reported for 4/6 at 24, 48 or 72 hours.

2. Death of 2/6 at 24 hours. The dose of the technical material applied was 0.05 ml per site or 0.2 ml per animal, this corresponds to appromimately 100 mg/kg. The 100 mg/kg level killed 2/6 animals in the dermal irritation study and the dermal LD_{50} study.

C. Conclusions

1. Classification of Data - Minimum

   a. Deficiency - The volume of the test material applied was 0.05 ml rather than the required dose of 0.5 ml. However, the application of the required dose of 0.5 ml would result in a dose greater than the acute dermal LD_{50} and has been considered in the evaluation of this study.

2. Toxicity Category IV for dermal irritation.

Technical Dyfonate 95.4%
Eye Irritation - Rabbit
Stauffer Chemical Co. Report T-6461 Feb. 12, 1979. Acc. 245491

A. Procedure

The test material 0.01 ml was applied into the congunctival sac in one eye of each of 9 New Zealand albino rabbits. The other eye served as an untreated control. The eyes of 3 animals was washed with 0.9% saline 30 seconds after exposure. With the remaining 6 animals the eye was not washed. The eyes were observed 24,48,72 and at 7 days and graded according to Draize.

B. Results

1. Moderate irritation at 24 hours for 1/6 unwashed eyes.

2. No deaths reported.

C. Conclusions

1. Classification of data - Minimum.

   a. Deficiency - The volume of the dose applied was 0.01 ml rather than the required dose of 0.1 ml. The application of the required dose of 0.1 ml of liquid would result in a dose corresponding to approximately 50 mg/kg. In the dermal toxicity study a dose of 30 mg/kg killed 1/6 animals. The dose applied has been considered in the evaluation of this study.

2. Toxicity Category - IV for eye irritation.

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Acute Oral Toxicity in Rats and Rabbits
(1979-1980)
Technical Dyfonate
-2-

Study	Material	Vehicle	EPA Asscession No.	Results	Toxicity Category	Core Grade	Study Reference
Acute oral LD50 male rabbit	95.6%	corn oil	243640	14.2 mg/kg	I	Minimum	T-6384
Acute oral LD50 female rabbit	95.6%	corn oil	243640	12.7 mg/kg	I	Minimum	T-6883
Acute oral LD50 male rat	95.4%	corn oil	243640	24.5 mg/kg*	I	Guideline	T-6461
Acute oral LD50 female rat	95.4%	corn oil	243640	10.8 mg/kg*	I	Guideline	T-6461

* Up graded from supplemental to guideline with additional data.

Acute Oral Toxicity in Rats and Rabbits
(1979-1980)
Dyfonate 20 Granular
-7-

Study	Material	Vehicle	EPA Accession No.	Results	Toxicity Category	Core Grade	Study Reference
Acute oral LD50 male rabbit	20 G	capsules	243640	59 mg/kg	II	Minimum	T-6384
Acute oral LD50 female rabbit	20 G	capsules	243640	66 mg/kg	II	Minimum	T-6384
Acute oral LD50 male rabbit	20 G	capsules plus corn oil	243640	79 mg/kg	II	Minimum	T-6384
Acute oral LD50 female rabbit	20 G	capsules plus corn oil	243640	83 mg/kg	II	Minimum	T-6384
Acute oral LD50 male rabbit	20 G	powdered in capsules	243640	73 mg/kg	II	Minimum	T-6384
Acute oral LD50 female rabbit	20 G	powdered in capsules	243640	59 mg/kg	II	Minimum	T-6384
Acute oral LD50 male rabbit	20 G	powdered in corn oil	243640	59 mg/kg	II	Minimum	T-6384
Acute oral LD50 female rabbit	20 G	powdered in corn oil	243640	58 mg/kg	II	Minimum	T-6384
Acute oral LD50 male rabbit	20 G	capsules	243640	12.7 mg/kg*	II	Minimum	T-6384
Acute oral LD50 female rabbit	20 G	capsules	243640	15.8 mg/kg*	II	Minimum	T-6384
Acute oral LD50 male rat	20 G	powdered in corn oil	243640	100 mg/kg	II	Guideline	T-6774
Acute oral LD50 female rat	20 G	powdered in corn oil	243640	43 mg/kg	I	Guideline	T-6774

*Calculated as active ingredient
*Up graded from supplemental to minimum with additional data.