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Shaughnessy No.:NEW CHEMICAL

Date Out of EAB: 20 MAY 1983

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Product Manager 25
Registration Division (TS-767)

From: Richard V. Moraski, Head (acting)
Review Section 1
Exposure Assessment Branch
Hazard Evaluation Division (TS-769c)

Attached please find the EFB review of...

Reg./File No.: 352-EUP-RRR

Chemical: Methyl 2-[[[[(4-methoxy,6-methyltriazin-2-yl)amino]-carbonyl]amino]sulfonyl]benzoate

Type Product: Herbicide

Product Name: DPX-T6376

Company Name: E.I. DuPont DeNemours & Co.

Submission Purpose: EUP - Use on wheat, barley and reduced tillage fallow.

ZBB Code:other

ACTION CODE: 710

Date In: 3/11/83

EFB #: 3272

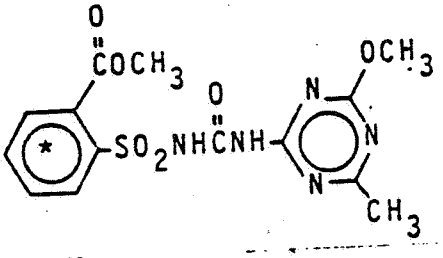
Date Completed: 5/20/83

TAIS (level II)	Days
63	4.0

1.0 INTRODUCTION

The registrant, DuPont, has requested an EUP (Reg. No. 352-EUP-RRR), to use the new herbicide DPX-T6376 on wheat, barley and reduced tillage fallow. According to EAB files, no data have previously been submitted in support of any uses of this chemical. Data were included in accession #071434.

2.0 STRUCTURE



Reference Name: DPX-T6376

Chemical Name: Methyl 2-[[[[(4-methoxy,6-methyltriazin-2-yl)amino] carbonyl]amino]sulfonyl]benzoate

3.0 DIRECTIONS FOR USE

Attachment 1 contains the complete (8 page) proposed labeling. Briefly, DPX-T6376 is a 60% dry flowable formulation which is applied in sufficient water to the target crops (barley, wheat and fallow land), either by ground (flat fan nozzles) or air (if raindrop or flood jet nozzles are used, higher spray volumes are recommended).

Applications may be pre- or post-emergence to control a wide variety of weeds. In-crop weed control is at rates of from 0.1 oz to 0.4 oz/ acre, depending on the variety of weed. Fallow treatment ranges from 0.1 to 0.8 oz/acre. Applications may be spring or fall. Watering-in is essential to proper action of the herbicide.

Total annual application may not exceed 0.8 oz/A.

Discussion: The label does not preclude the planting of other follow-on crops, in rotation with the experimental crop, although the notation is made that "bioassays" might show residual activity even 2 years postapplication. We assume that any residues in the target crops will be covered by the requested tolerances.

Recommendation: The label should bear a 2-year restriction against the planting of any other crops in rotation with the target crops, or, alternatively, should bear a crop destruct warning for such crops.

4.0 PHYSICAL AND CHEMICAL PROPERTIES

Attachment 2 contains the complete set of product data sheets.

Discussion: The product data sheets appear to be thorough and complete.

5.0 PROPOSED EXPERIMENTAL PROGRAM

Attachment 3 contains a copy of the proposed experimental program.

In brief, the herbicide will be applied within 6 distinct, small grain growing regions of the U.S., encompassing 34 states. The program will run for 3 years, with a total of 750 lbs. a.i. being used in the program. Total treatment acreage will not exceed 5000, 10000 and 15000 acres for years 1 through 3, respectively.

The largest single use sites and amounts are ND (6000A, 150 oz), WA (2600A, 65 oz), MT (3000A, 75 oz), SD (3000A, 75 oz), KS (3600A, 90 oz), OK (2400A, 60 oz), and TX (2000A, 50 oz).

Point-of-contact in each state are included.

Discussion: The proposed experimental program seems reasonable, considering the geographic latitude of the coverage, especially since the unit application rates are relatively low.

6.0 DATA TO SUPPORT EUP

Current EF data requirements for this use on field crops include hydrolysis, aerobic soil metabolism, accumulation in rotational crops and accumulation in fish (flow-through study).

Discussion: If the label bears either a 2 year rotational crop restriction, or equivalent crop destruct warning, this data requirement may be waived, for purposes of the EUP.

No flow-through fish accumulation study was included with this submission. Due to the apparent long hydrolytic halflife, a waiver of this data requirement does not seem likely.

6.1 Friedman, P. 1982. Hydrolysis of ^{14}C-phenyl-DPX-T6376. Document No. AMR-62-82. E.I. Du Pont de Nemours and Company. Biochemicals Department. Research Division. Experimental Station. Wilmington, Delaware 19898. (company confidential)

Experimental

DPX-T6376 was synthesized and radiolabeled in the phenyl ring. Specific activity was 8.6 uCi/mg with a radiopurity of 98%.

A 5 ppm stock solution in distilled water was prepared, and suitably diluted to 0.5 ppm as needed. Aliquots (300 ml) were buffered to pH 5, 7 or 9 and incubated in the dark at either 15° or 25°C. Aliquots (20 ml) were withdrawn on day 0, 1, 2, 5, 7, 9, 14, 21, and 30.

Total radioactivity was determined by extraction with methylene chloride, concentration, and LSC quantification. This was followed by HPLC quantification of the parent and "primary" degradate (methyl-2-(aminosulfonyl)benzoate). Polar products were suitably extracted, concentrated, counted and quantified. A single peak was identified as saccharin by comparision of the retention time against a known standard. Confirmation was by MS.

Results and Discussion

No hydrolysis was measured in either the pH 7 or 9 tests, at either temperature. Halflife at ph 5 and 25°C was about 3 weeks, and at 15°C, greater than 30 days. The "primary" degradation product methyl-2-(aminosulfonyl)benzoate was found to demethylate under acidic conditions, followed by ring closure to form saccharin. Total radioactivity throughout the experiment remained constant.

Conclusions: In recomputing the halflives based on the reported data, we confirmed the 3 week estimate for pH 5 and 25°C. However, the actual halflife at pH 5 and 15°C ranged from 74 to 101 days (5.0 ppm vs 0.5 ppm), suggesting that parent DPX-T6376 is persistent in water, even under acidic conditions.

This study was reasonably well done. However, no monitoring for the triazine fragment of the parent molecule was reported. We cannot accept this study until the fate of this component has been clarified.

Recommendation: The registrant should be requested to provide details of the fate of the triazine moiety under conditions of hydrolysis.

6.2 Friedman, P. 1982. Aerobic Soil Metabolism of ^{14}C-phenyl-DPX-T6376. Document No. AMR-75-82. E.I. Du Pont de Nemours and Co. Biochemicals Department. Research Division. Experimental Station. Wilmington, Delaware 19898. (company confidential)

Experimental

A 51 ppm stock solution (in acetone) of DPX-T6376 was prepared, diluted to 5 ppm with acetone. One ml of each of these solutions was added to two 50 gm (dry weight) aliquots of a Keyport silt loam, having the characteristics shown in attachment 4, to simulate 1.0 and 0.1 ppm treatments.

Sterile soil (autoclaved as 15 PSI for 1 hour x 3 days) was similarly treated.

All soils were maintained at 70 % moisture holding capacity throughout the experiment.

Soils were placed in a 250 ml biometer flask, from which CO_2 was trapped in 0.1 N NaOH. Caustic was changed weekly.

Analysis of the caustic for CO_2 was via $BaCl_2$ precipitation followed by LSC of both precipitate and supernatant.

Analyses of soils was performed for both parent and metabolites at for weeks 0, 1, 2, 4, 8, 16 and 24 by multiple extraction with solvent followed by LSC and HPLC as in the Hydrolysis experiment reviewed earlier.

Results and Discussion

Estimated aerobic soil halflife was 2 to 3 weeks, with the major metabolite (36%) being $^{14}CO_2$ after 24 weeks. Metabolites identified were methyl 2-(aminosulfonyl)benzoate, 2-(aminosulfonyl)-benzoic acid and Saccharin. Structures are shown in attachment 5. Polar degradation products were identified as saccharin and 2-(aminosulfonyl)benzoate.

In the sterile soil, only 3 to 4% of the applied parent was found after 24 weeks. No CO_2 was produced. Major metabolites were methyl 2-(aminosulfonyl)benzoate, 2-(aminosulfonyl)benzoic acid, the reported hydrolytic products.

Conclusions: In recomputing, EAB determined a halflife of 3.7 and 4.0 weeks for the 1.0 and 0.1 ppm experiments, respectively, suggesting that parent DPX-T6376 is moderately persistent under aerobic soil conditions.

This study was reasonably well done. The statistics looked very good. However no monitoring for the triazine fragment of the parent molecule was reported. We cannot accept this study until the fate of this component has been clarified.

Recommendation: The registrant should be requested to provide details of the fate of the triazine moiety under conditions of aerobic soil metabolism.

6.3 Chrzanowski, R.L. 1982. ^{14}C-DPX-T6376. Aerobic Soil Dissipation Study in the Greenhouse. Document No. AMR-89-82. E.I. Du Pont de Nemours and Co. Biochemicals Department. Research Division. Experimental Station. Wilmington, Delaware 19898. (company confidential)

Introduction

^{14}C-benzene-ring labeled DPX-T6376 was prepared and was found to have a specific activity of 8.62 uCi/mg with a radiochemical purity of 99%. Authentic standards of anticipated degradation productes were prepared:2-(aminosulfonyl)benzoic acid, Methyl 2-[(aminocarbonyl)aminosulfonyl]benzoic acid, methyl-2-(aminosulfonyl) benzoate and saccharin.

Analysis of each of the standards involved diazotization with diazomethane, followed by GC/MS isolation and quantification. Anomalously, all degradates appeared to degrade to saccharin (either as the N-methyl or O-methyl derivatives) under the conditions of the analysis.

Experimental

Three soils were used in this study: a sandy loam and two silt loams. Soil characteristics appear in attachment 6. 50 gm aliquots of each soil were placed into 12 150 ml glass beakers each, to a depth of 1.25". Methylene chloride solutions (180 ml) of ^{14}C DPX-T6376 were added to each beaker by syringe. This was reported to be equivalent to an application of 100 g ai/Ha.

One beaker was set aside for analysis. The others were placed in a greenhouse and water added to maintain 75% of moisture holding capacity. Lighting intensity was not specified.

Individual samples were taken on days 0, 1 and 2, and after weeks 1, 2, 4, 8, and 14 and analyzed for total parent and degradation product radioactivity by solvent extraction followed by LSC. Specific degradates were identified by cochromatography with the authentic non-radioactive standards.

Results and Discussion

Under greenhouse condition, soil halflife was reported to average 10 days. The majority of methylene chloride extractable material was found to be residual parent and methyl-2-(aminosulfonyl) benzoate. The extracted aqueous phase contained mostly saccharin (50 to 99%) and Methyl 2-[(aminocarbonyl)aminosulfonyl]benzoate.

Conclusions: In recomputing, EAB determined halflives were 2.4, 3.4 and 2.8 weeks for the Fallsington Sandy Loam, Flanagan Silt Loam and Keyport Silt Loam experiments, respectively. This suggests that parent DPX-T6376 is moderately persistent under greenhouse conditions.

This study was reasonably well done. The statistics looked very good. There were, however, a number of deficiencies which may invalidate the work:

- °° neither sterile nor dark controls were provided.
- °° the intensity of the incident light was not specified.
- °° the temperature at which the experiment was conducted was not specified.
- °° no monitoring was done for the triazine fragment of the parent molecule.
- °° The thermolability of the various degradates appears to invalidate the use of diazotization as an analytical tool relative to the MS portion of the experiment.

Recommendation: The registrant should be requested to respond to the deficiencies noted above.

7.0 EXECUTIVE SUMMARY

The product chemistry summary sheets appear to be complete. The label deficiencies were noted earlier. The experimental program is reasonable, and acceptable to EAB.

Parent DPX-T6376 appears refractory to hydrolysis under neutral and alkaline conditions, but slowly hydrolyses in acidic media with a halflife of up to 101 days under ambient temperature conditions.

Aerobic soil metabolism studies suggest a soil halflife of parent DPX-T6376 of 3.7 to 4 weeks in one study, and for 2.4 to 3.4 weeks in another. Major degradates include methyl-2-(aminosulfonyl) benzoate, saccharin and Methyl 2-[(aminocarbonyl)aminosulfonyl] benzoate.

8.0 CONCLUSIONS

We cannot concur with the proposed EUP at this time due to the numerous deficiencies in the submitted studies as well as the outstanding fish accumulation data requirement.

9.0 RECOMMENDATION

The registrant should be requested to address the deficiencies noted for each study.

The issue of accumulation in fish should be addressed, either in rebuttal, or by submission of a suitable study.

The proposed label should bear the appropriate 2-year rotational crop restriction, or a suitable crop destruct warning.

Emil Regelman
Chemist
EAB/HED (TS-769c)
May 20, 1983

Pages 9 through 37 contain detailed registration data submitted by the registrant. These pages are not included.