To: Robert Taylor  
Product Manager 25  
Registration Division (TS-767)

From: Samuel Creeger, Chief  
Review Section #1  
Exposure Assessment Branch  
Hazard Evaluation Division (TS-769)

Attached, please find the EAB review of...

Reg./File #: 352-EUP-111
Chemical Name: DPX T6376
Type Product: Herbicide
Product Name: ALLY
Company Name: DuPont
Purpose: EUP on Cereals: Resubmission

ZBB Code: ?  
Action Code(s): 714  
Date Received: 4/26/84  
Date Completed: 7/12/84

EAB #(s): 4316  
TAIS Code: 52
Total Reviewing Time: 5.0 days

Deferrals to:  
Ecological Effects Branch  
Residue Chemistry Branch  
Toxicology Branch
1.0 INTRODUCTION

In the EAB review of 5/20/83, numerous deficiencies were found in
the submitted data, resulting in an EAB non-concurrence with the
EUP request. To date, these deficiencies have not been addressed.

DuPont has now submitted additional data to support the EUP use
of ALLY Herbicide (Methyl 2-[[[(4-methoxy,6-methyltriazin-2-yl)-
amino]carbonyl]amino)sulfonyl]benzoate) on Wheat, Barley and
reduced tillage fallow.

2.0 STRUCTURE, DIRECTIONS FOR USE and EXPERIMENTAL PROGRAM

See review of 5/20/83.

3.0 SUBMITTED DATA

3.1 Friedman, P.L. Undated. Hydrolysis of 14C-4-methoxy-6-methyl-
1,3,5-triazin-2-amine. Document No. AMR-136-83. (Company confi-
dential) E.I. DuPont de Nemours and Co. Experimental Station.
Wilmington, DE. 9 pages, 4 figures. No references

Introduction

The hydrolysis of 14C-4-methoxy-6-methyl-1,3,5-triazin-2-amine
was studied at 25°C, in sterile buffer solutions of pH 5,7 and 9.

Experimental

14C-4-methoxy-6-methyl-1,3,5-triazin-2-amine was prepared, and
found to be 99% radiopure with a specific activity of 35.4 uCi/mg.
Stock solutions at 0.5 and 5.0 ppm were prepared in pHydrion
Buffer Solutions of pH 5,7 and 9, which had been previously
autoclaved for 1 hour on 3 consecutive days. All glassware had
been similarly autoclaved.

Solutions were stored in glass stoppered Erlemeyer flasks in
a dark autoclave at a constant 25°C, with 20 ml aliquots being
taken on days 0, 1, 2, 5, 7, 14, 21 and 30.

Analysis for total radioactivity was by LSC counting. Component
separation was attempted by HPLC using acetonitrile/water mobile
phase (5/95, v/v) on a PRP column. Structures for the two peaks
detected are appended to this review. Confirmation was by co-
chromatography with unlabeled compounds, as well as by TLC separa-
tion using precoated silica gel 60 F-254 plates and a methylene
chloride/methanol/ammonium hydroxide (144/50/8, v/v/v) mobile
phase. Peak quantification was by fluorescence quenching (unla-
beled compounds) and by Automatic TLC-Linear Analyzer for the
radiolabeled compounds.
Results and Discussion

The 4-methoxy-6-methyl-1,3,5-triazin-2-amine was found to be very stable to hydrolysis at all pH's, with between 96 and 105% of the original material found unchanged at the end of the experiment. A minor (<2%) component (the 4-amino-6-methyl-1,3,5-triazin-2-ol) was detected in the high concentration test.

Conclusion

This study was scientifically valid, and is acceptable to EAB. Neither sample chromatograms nor copies of TLC plates were included with this study.

This study satisfactorily addresses EAB concerns raised in the 5/20/83 review.

EAB therefore considers the hydrolysis data requirement satisfied.


Introduction

This study, of the rate of degradation of DPX-W4189 (chlorosulfuron, 2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino-carbonyl]benzenesulfonamide) (Shaughnessy # 118601) in two soil types, was submitted in support of an EUP usage on barley and wheat, and was reviewed on 11/17/80.

Its inclusion in the current submission stems from the 6/8/83 meeting between the registrant and EAB concerning the fate of the triazine moiety of DPX T6376. At that time, EAB agreed that both aerobic metabolism and field dissipation studies of chlorosulfuron would be adequate to delineate the rate of formation and decline of that moiety, which is identical to that in DPX T6376.

Discussion

This study was found acceptable in support of the proposed EUP in the 11/17/80 review.

A reevaluation of the reported data (see table 7, appended) indicates that the concentration of the aminotriazine moiety peaked at about 1 month, then declined slowly. Estimated half-lives were 6 months ($r^2=0.98$) and 10.3 months ($r^2=0.52$) for the 0.1 and 1.0 ppm solution, respectively. The latter data are too unreliable to use in estimating the rate of dissipation.
Conclusion

This study adequately addresses one of the earlier EAB concerns (the triazine moiety). However, a number of specific deficiencies were noted in the review of 5/20/83 which have still not been addressed. These questions must be satisfactorily resolved prior to EAB concurrence with full registration. See the 7/24/83 review, Section 6.3.

This study and the one reviewed on 5/20/83 are adequate to support the proposed EUP.

3.3
Han, J. C-Y. Undated. 14C DPX-W4189 Soil Disappearance Studies in the Field. Document No. AMR-54-81. (company confidential) E.I. DuPont de Nemours and Co. Experimental Station. Wilmington, Delaware. 7 pages, 3 tables, 1 figure. 3 reference

Introduction

This study, of the rate of degradation of DPX-W4189 (chlorosulfuron, 2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino- carbonyl]benzenesulfonamide) (Shaughnessy # 118601) in five soil types under field conditions was submitted in support of an EUP usage on barley and wheat, and was reviewed on 11/17/80.

Its inclusion in the current submission stems from the 6/8/83 meeting between the registrant and EAB concerning the fate of the triazine moiety of DPX T6376. At that, EAB agreed that both aerobic metabolism and field dissipation studies of chlorosulfuron would be adequate to delineate the rate of formation and decline of that moiety, which is identical to that in DPX T6376.

Discussion

This study was found acceptable in support of the proposed EUP in the 11/17/80 review.

A reevaluation of the reported data (see table 3, appended) indicates that the concentration of the aminotriazine moiety was only monitored in the Newark, DE portion of the study, and not in the other 4 soils tested. The data suggest that this moiety peaks at about 4 weeks, then declined slowly. Estimated half-life was 48 weeks (r^2 = 0.32). This data is too unreliable to use in estimating the rate of field dissipation.

Conclusion

This study cannot be used to support the field dissipation of the triazine moiety of DPX-T6376. The field dissipation data requirement must be adequately addressed prior to EAB concurrence with full registration (this study is not required in support of the proposed EUP).
Introduction

Possible bioaccumulation of DPX T6376 was estimated using flow-through aquaria and bluegill sunfish.

Experimental

Two glass aquaria were filled with "fresh" water, and amended with $^{14}$C-phenyl-labeled DPX T6376 at 1.0 and 0.01 ppm, respectively (0.086 and 8.62 uCi/mg, at >98% radiopurity). A third aquarium served as control. Conditions were maintained as follows: 23 +/- 1°C, pH 7.2-7.7, total alkalinity 101.8 +/- 3.5 mg/L (as CaCO$_3$) and O$_2$ 6.4 +/- 0.8 ppm (via constant aeration). Water turnover rate was 4-6x/day. Average DPM/ml for the radio-DPX were 195 and 187, respectively.

Throughout the experiment, radio-levels in solution were maintained very close to nominal values.

A total of 70 bluegill sunfish were added to each tank, with removal of 4 fish and 100 ml water at 0, 1 and 3 days, 1, 2, 3 and 4 weeks. Depuration consisted of transfer of the remaining fish in the treatment tanks to two undosed aquaria, with sampling on days 1, 3, 7, 10 and 14.

Analysis was by dissection of the fish into carcass, viscera and liver, followed by (storage until) combustion and LSC quantification. Water samples were analysed by both LSC and TLC for peak identification.

Results and Discussion

Throughout the test period, parent DPX-T6376 represented >95% of the material in solution, with <5% consisting of methyl-2-(aminosulfonyl)benzoate and saccharin.

Highest biomagnification was seen in the liver and viscera at 2 to 4x. Depuration was rapid, with >95% excretion over the test period.

Conclusion

This study appears to be scientifically valid. DPX T6376 does not appear to bioaccumulate in bluegill sunfish.
This study is incomplete, and therefore cannot be accepted as is. Specific deficiencies include failure to specify the method used in dosing the aquaria, and failure to submit sample TLC chromatograms and raw TLC counting data. It was also not reported whether any fish died in any of the test groups.

The possibility exists that the data may be statistically unreliable due to low sample counts. This must be confirmed by review of the above cited data.

4.0 CONCLUSIONS

Experimental Program: Reviewed on 5/20/83 and found acceptable.

Directions for Use: Reviewed on 5/20/83 and found acceptable.

Hydrolysis: DPX-T6376 does not appear to hydrolyze appreciably at all pH values tested. Data requirement has been satisfied, although several deficiencies should be addressed prior to full registration.

Aerobic Soil Metabolism: One study (Friedman. 1982. Aerobic Soil Metabolism of 14C-phenyl-DPX-T6376. Document #AMR-75-82) had been previously submitted, reviewed and found acceptable with one deficiency (addressed below).

The current submission included an aerobic soil metabolism study previously submitted and found in support of the DPX-4189 (GLEAN) registration (C. Rapisarda. Undated. Microbial Degradation of 14C DPX-4189 in Soil. Document No. AMR-43-81) which was rereviewed to ascertain the fate of the major triazine degrade in soil. It was found that about half of the reported data on the decline of the triazine moiety were statistically unreliable, and therefore unacceptable. The remaining data appear reliable, and indicate a soil halflife of about 6 months.

This data adequately addresses earlier EAB concerns. Therefore, this data requirement is considered satisfied.

Field Dissipation: The current submission also included a study previously submitted and found acceptable in support of the DPX-4189 (GLEAN) registration (Han, J. C-Y. Undated. 14C DPX-W4189 Soil Disappearance Studies in the Field. Document No. AMR-54-81) which was rereviewed to ascertain the fate of the major triazine degradation soil under field conditions.

This study provided no useful data. However, this study is not required to support the proposed EUP.

Accumulation in Fish: One study was reviewed with this submission, and found acceptable in support of the EUP. A number of deficiencies were identified, which must be addressed before EAB can concur with full registration.
Rotational Crop: No data have yet been submitted to support this data requirement. As noted in the review of 5/20/83, the label must 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.

5.0 RECOMMENDATION

EAB concurs with the proposed EUP use on wheat, barley and reduced tillage fallow.

The registrant should be notified of the numerous deficiencies noted in this and the earlier review, and should be requested to address them prior to requesting full registration for this product.

Emil Regelman
Chemist
EAB/HED
July 12, 1984
FIGURE 1

STRUCTURE OF TEST COMPOUND AND HYDROLYSIS PRODUCT

4-methoxy-6-methyl-1,3,5-triazin-2-amine

4-amino-6-methyl-1,3,5-triazin-2-ol

* denotes the position of the $^{14}C$ label which is the carbon atom adjacent to the amine group.
### TABLE III (Cont'd)

**C. Newark, Delaware (\(^{14}\)C-Triazine-DFX-H4189)**

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<th>Exposure Time (wk)</th>
<th>Soil Depth (cm)</th>
<th>((\text{NH}_4\text{)}_2\text{CO}_3/\text{H}_2\text{O}/\text{MeOH}) Extract</th>
<th>Unextracted Residue</th>
<th>(^{14})C-Residues Found, % of Applied</th>
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<td>(\text{H}_2\text{O}) Phase</td>
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### Table: Change of C-TRIazine Labeled DPX-4189 in Reagent Silt

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#### Notes:
- **C-TRIazine Labeled DPX-4189 in Reagent Silt**
- **Table Legend:**
  - **C-TRIazine Labeled DPX-4189**
  - **Reagent Silt**
  - **ppm**

#### Analysis:
- The table represents the change in C-TRIazine labeled DPX-4189 in reagent silt over a range of ppm concentrations.
- The data suggests no observable change in concentration across the tested samples.

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### Scatter Diagram

- **X-axis:** ppm
- **Y-axis:** Change of C-TRIazine Labeled DPX-4189 in Reagent Silt

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### Equation

- The equation for the change in C-TRIazine Labeled DPX-4189 in reagent silt is not explicitly provided in the text. It appears to be a negligible change.