128887

Shaughnessy No.: ~~N/A~~ 073791

Date Out of EAB: SEP 18 1986

To: R. Mountfort
Product Manager 23
Registration Division (TS-767)

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

Attached, please find the EAB review of...

Reg./File # : 352-EUP-RGN

Chemical Name: DPX-L5300

Type Product : Herbicide

Product Name : DPX-L5300

Company Name : Du Pont

Purpose : New Chemical, EUP on wheat and barley

Action Code(s): 710 EAB #(s) : 5907

Date Received: 9/5/85 TAIS Code:

Date Completed: SEP 18 1986 Total Reviewing Time: 7.0 days

Deferrals to:

____ Ecological Effects Branch

____ Residue Chemistry Branch

____ Toxicology Branch

ACC# 073786 = MRID 00148630

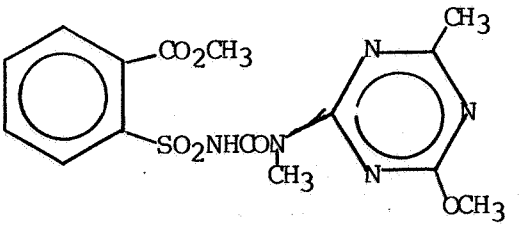
ACC # 073791 = MRID 148645 TO 148654 AND 149672

1/29

1.a CHEMICAL:

Methyl 2-[[[N-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)-N-methylamino]carbonyl] amino sulfonyl]benzoate.

DPX-L5300



1.b Physical Properties:

Molecular Weight: 395.39
Density: 1.54 gm/cc
Melting Point: 141°C
Vapor Pressure at (?)°C: 2.7×10^{-7} mm Hg Note absent information!
Octanol/Water Partition Coefficient:

282 at pH 1.5
181 at pH 4.0
100 at pH 5.0
18 at pH 6.0
0.36 at pH 7

Solubility in Water at 25°C:

pH	mg/l
4.0	28
5.0	50
6.0	280

2. TEST MATERIAL:

^{14}C-(Triazine)-DPX-L5300

^{14}C-(Phenyl(U))-DPX-L5300

3. STUDY/ACTION TYPE:

Application for an Experimental Use Permit for DPX-L5300 as an Herbicide on wheat and barley.

4. STUDY IDENTIFICATION: Acc #'s 073786 and 073791.

oo Water/Octanol Partition Coefficient of [Phenyl-^{14}C(U)] DPX-L5300 by H.Y. Mohammed (AMR-407-85).

oo Hydrolysis of [Phenyl-^{14}C(U)]- and [Triazine-2-^{14}C] DPX-L5300 by E.M. Venzon

oo Aerobic Soil Metabolism of [Triazine-2-^{14}C]-DPX-L5300 by C. Rapisarda (Interim Report, AMR-360-85)

oo Soil Column Leaching Study of [Phenyl-^{14}C(U)] DPX-L5300 by A.C. Barefoot (AMR-404-85)

oo Batch Equilibrium (Adsorption/Desorption) and Soil Thin Layer Chromatography Studies with ^{14}C DPX-L5300 (Listed but not included for review).

5. REVIEWED BY:

Akiva D. Abramovitch, Ph.D.
Chemist
Environmental Chemistry Review Section 1/EAB/HED/OPP

Abramovitch
Date: SEP 18 1986

6. APPROVED BY:

Samuel M. Creeger, Chief
Supervisory Chemist
Environmental Chemistry Review Section 1/EAB/HED/OPP

Sam M Creeger
Date: SEP 18 1986

7. CONCLUSIONS:

Required data for the experimental use permit of DPX-L5300 herbicide are as follows:

Data Requirement	Satisfied
Hydrolysis	Yes
Aerobic Soil Metabolism	No
Accumulation in Fish	Yes (waived)
Leaching	Yes
Rotational Crop Data	No

Hydrolysis:

The hydrolysis study satisfied the EAB data requirement. DPX-L5300 hydrolyzed at 25°C with half lives shown in the following table:

Temperature (°C)	pH	Half Life (day) 5	7	9
25		<1	3-6	(a)

(a) very slow hydrolysis (see 10.1.C)

The hydrolysis products were methyl 2-(aminosulfonylmethyl)benzoate and 2-methoxy-N,6-dimethyl-1,3,5-triazin-2-amine. In addition to the major hydrolysis products, saccharin, low levels (1-6%) of 4-methylamino--6-methyl-1,3,5-triazine-2-ol (sulfonamide) and 4-methylamino-6-methyl-1,3,5-triazin-2-ol (O-demethyl triazine amine), were formed due to further degradation of the primary degradates.

Aerobic Soil Metabolism:

The aerobic soil degradation study can satisfy the EAB data requirement for an EUP pending the completion of the study and submission of final report. DPX-L5300 degraded in the Gardena and Keyport silt loam soils with first half lives of 1-6 days via hydrolysis as the major degradation pathway (see hydrolysis).

Batch Equilibrium and Soil TLC:

The study was not included with this review (though it was listed in the table of contents).

Leaching:

The leaching experiment satisfied the EAB data requirement. The data indicated that DPX-L5300 leaches quite readily and might enter ground water.

Octanol/Water Partition Coefficient:

The octanol/water partition coefficient was determined as 0.3 at pH 7.

Fish Accumulation:

A fish accumulation study was not submitted and a waiver was requested based on the water/octanol partition coefficient of 0.3. Since correlation between octanol/water partitioning and fish accumulation is only accurate within a factor of 100, our position will be that DPX-L5300 and its degradation products have potential to accumulate in fish to levels 30 times higher than levels in water. In light of this position, the registrant may want to conduct a fish accumulation study if they feel an actual study will show a lower accumulation factor.

8. RECOMMENDATIONS:

The hydrolysis and the leaching data requirements have been satisfied. The request to have the fish accumulation study waived was accepted based on the low octanol/water partition coefficient. The soil degradation study can satisfy the EAB data requirement for the EUP pending successful completion of the study and submission of a final report. Meanwhile, it is in the reviewer's opinion that the pending completion of the soil degradation study should not be the sole cause for delay in granting an EUP in view of the presently available information with regard to the fast degradation of DPX-L5300 in the two soils studied and in water and due to the low application rate. Rotational crop data or a label restriction against planting rotational crops in treated fields is also needed.

9. BACKGROUND:

A. Introduction:

Du Pont has applied for an experimental permit for DPX-L5300 for use as an Herbicide on wheat and soybeans.

B. Directions for Use:

DPX-L5300 Herbicide is a dry flowable powder containing 75% of the active ingredient (25% inert ingredients). The herbicide will be sprayed via ground (5 gallons water solution per acre) or aerial equipment (1 gallon water solution per acre) for selective post emergence weed control in wheat and barley. An application of 1/6-2/3 oz of DPX-L5300 per acre is recommended.

10 DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

10.1 A. Study Identification: Hydrolysis of ^{14}C-DPX-L5300.

The study was conducted by E. M. Venzon at the Agricultural Chemicals Department, Experimental Station of Du Pont (Document No. AMR 385-85).

B. Test Materials and Methods:

Solutions containing approximately 500 ppm of [Phenyl-^{14}C] DPX-L5300 were prepared by dissolving 10.2 mg of the radiolabeled DPX-L5300 (20.5 microCi/mg, 97% radiochemical purity) in 5 ml of acetone and diluting it to 20 ml with 15 ml of sterilized water. A second sample was prepared in a similar fashion with 10.5 mg of [triazine-2-^{14}C] DPX-L5300 (10.6 microCi/mg, 98% radiochemical purity). Aliquots were then added to sterilized buffered solutions of pH's 5, 7 and 9 (pHydrion Buffer, Metrepak, for pH 5 and 0.01 M boric acid for pH 7 and 9) to prepare 1 and 10 ppm test solutions of DPX-L5300 (all glassware were also sterilized). Each test solution was placed at 25°C in the dark and aliquots were drawn after 0, 4, 6, 14, 21 and 32 days of incubation of the phenyl labeled DPX-L5300 and 0, 1, 4, 7, 13, 21 and 33 for the triazine labeled DPX-L5300. The total amount of radioactivity in each sample was counted by LSC. Aliquots were extracted with methylene chloride for analysis. The identity of the hydrolysis products was determined by co-chromatography on TLC and HPLC with authentic samples and additional confirmation was obtained by direct probe mass spectrometry of the extract using electron impact ionization.

C. Reported Results:

Temerature (°C)	Half Life (days)		
pH	5	7	9
25	<1	3-6	slow

DPX-L5300 hydrolyzed very fast at pH 5 at 25°C in the dark and only 1% of the parent compound remained intact after 1 day. At pH 9, hydrolysis occurred very slowly and 87-95% of the parent compound was intact after 32 days. At pH 7, first order half lives of 3-6 days were calculated for DPX-L5300. The hydrolysis products were methyl 2-(aminosulfonylmethyl)-benzoate and 2-methoxy-N,6-dimethyl-1,3,5-triazin-2-amine. In addition to the major hydrolysis products, saccharin, low levels (1-6%) of 4-

methylamino-6-methyl-1,3,5-triazine-2-ol (sulfonamide) and 4-methylamino-6-methyl-1,3,5-triazin-2-ol (O-demethyl triazine amine), were formed as a result of secondary degradation of the primary degradates. About 1-7% of the total radioactivity at pH 5 was present as several unidentified polar compounds. The experiment provided a quantitative account for the total amount of the radioactive material.

D. Study Author's Conclusions:

No additional conclusions to those stated in the result section. The author observed decomposition in all the 0 day samples and attributed it to the instability of the parent compound even in organic solvents. With that in mind, day 0 samples were used for half life determination.

E. Reviewer's Discussion and Interpretation of Results:

The study was accepted in fulfillment of the hydrolysis data requirement. A fast hydrolysis was noted under acidic and neutral conditions with half lives of less than 6 days. However, under basic conditions (pH 9) hydrolysis of DPX-L5300 was slow.

10.2 A. Study Identification: Aerobic Soil Metabolism of [Triazine-2-^{14}C] DPX-L5300 (Interim Report).

The study was conducted by C. Rapisarda of the Agricultural Chemicals Division of Du Pont, Research Division Experimental Station, Wilmington, Delaware (Document No. AMR-360-85).

B. Materials and Methods:

A solution of ^{14}C-triazine-DPX-L5300 was prepared in aqueous solvent containing 85.5 ml of distilled and deionized water, 4.5 ml of 0.01 M potassium phosphate pH 7 buffer, 9 ml of acetone and 1 ml of aqueous ammonium carbonate. The [^{14}C-triazine] DPX-L5300 had a specific activity of 4.7 microCi/mg and 99% radiochemical purity. DPX-L5300 did not undergo significant decomposition in the above solution upon 7 weeks of storage. Soil samples of fresh Keyport silt loam (0-6" deep) were taken from Newark, Delaware and Gardena silt loam from Rodgers, North Carolina and allowed to dry for three days before analyzed. Portions of the soils were sterilized in autoclaves for one hour at 15 psi steam for three consecutive days. Duplicate 50 gm oven dry sterile and non-sterile soil samples were weighed into a 250 ml biometer flask with connecting side arm containing 10 ml of 0.1N NaOH to trap evolved $^{14}CO_2$. All soils were fortified with a test aqueous solution described above containing 3.0 microgram (0.14 microCi) of the ^{14}C-triazine-DPX-L5300 to simulate the maximum recommended field use of 70 gm a.i./ha. Additional water was added to the soil to maintain 70% of the field moisture capacity. The soils were thoroughly mixed with a spatula, oxygen was introduced and the flasks were sealed and incubated in the dark at 25°C. Aliquots from the caustic solution in the side arm were analyzed periodically by LSC. Radioactive carbon dioxide was precipitated for analytical purposes as barium carbonate by treatment with barium chloride. Non-sterile soil samples were taken after 0, 1, 2, 5, 9, 14, 21, 28, 42, 56, 84 and 112 days of incubation and extracted three times with 100 ml aliquots of Acetone/0.1 M $(NH_4)_2CO_3$ (9/1 by volume). The combined extracts counted

by LSC for total radioactivity. The extracts were concentrated on a rotary evaporator under reduced pressure to about 0.5 ml for chromatographic analysis by TLC in reference to authentic samples. Extracted soils were combusted and the generated $^{14}CO_2$ analyzed.

C. Reported Results:

DPX-L5300 degraded rapidly in sterile and non-sterile Keyport and Gardena silt loam soils, maintained at 70% of their field moisture capacity and incubated in the dark at 25°C. In non-sterile Keyport silt loam (pH 4.3), DPX-L5300 degraded with first half life of less than 1 day while in non-sterile Gardena silt loam soil (pH 7.5) the first half life was about 6 days. The degradation was basically hydrolytic and was more rapid in acidic soils as anticipated from the hydrolysis study. DPX-L5300 degraded slightly faster in sterilized soils than in non-sterilized soils since the sterilized soils were slightly more acidic. Generation of $^{14}CO_2$ was negligible within the study period. An almost quantitative account was provided for the initially applied radioactivity in both extracted ^{14}C material and ^{14}C soil residues. The degradates were identical to those obtained in the hydrolysis study and included also N-demethyl triazine amine in addition to the products listed in the hydrolysis product. The proposed metabolic pathway of DPX-L5300 is attached to this report.

D. Study Author's Conclusions:

The author concluded that the DPX-L5300 underwent fast degradation in both sterilized and non-sterilized soils and proceeded faster in acidic soils. The degradation pathway was hydrolysis and only negligible quantities of $^{14}CO_2$ was generated due to low microbial degradation.

E. Reviewer's Discussion and Interpretation of Study Results:

The study appeared to generate valid scientific results and should satisfy the EAB data requirement pending the completion of the study and submission of final report. It is in the reviewer's opinion that further confirmations of the identity of the degradates should be obtained by co-chromatography on HPLC as provided by the enclosed hydrolysis study.

10.3 A. Study Identification: Batch Equilibrium (Adsorption/Desorption) and Soil Thin Layer Chromatography Studies with ^{14}C- DPX-F5384.

B. Material and Methods: N/A

C. Reported Results: N/A

D. Study Author's Conclusions: N/A

E. Reviewer's Conclusions and Interpretation of Study Results:

The study was not included with this submission (the aerobic soil metabolism study was included in both section 9 and 11).

10.4 A. Study Identification: Soil Column Leaching Behavior of [Phenyl-^{14}C(U)] DPX-L5300.

The study was conducted by A. C. Barefoot of the Agricultural Chemicals Department, Research Division Experimental Station of Du Pont (Document No. AMR-404-85).

B. Materials and Methods:

Fargo silty clay, Sassafras loamy sand, Keyport silt loam and Gardena silt loam (see attached characteristics) were sieved and packed to a height of 12" into a 2" diameter chromatography columns, filled with water to a height of 8". A 1 liter reservoir was used to introduce the water eluant. The [Phenyl-^{14}C(U)] DPX-F5300 (0.02 mg, 0.4 microCi) in acetonitrile was applied via a microliter syringe. Then a layer of sand was added to protect the column during the addition of water. Water was then added slowly to the column (in 0.4" aliquots) until the 1 liter reservoir was consumed (20" of water). Aliquots collected (20 ml) were examined by LSC for total radioactivity and selected samples were co-chromatographed on HPLC with authentic samples of DPX-L5300 and samples of degradates obtained in the soil degradation study. Soils were removed from the column from the top in 2 inch segments and the amount of radioactivity in each segment was determined by combusting the soil and quantitating the generated $^{14}CO_2$. Selected soil samples were extracted with successive aliquots of acetone/0.1M ammonium carbonate (90:10) and the extracts were analyzed by LSC for total radioactivity. Extracts were concentrated almost to dryness, redissolved in acetonitrile and co-chromatographed on silica gel TLC. Unextracted residues were determined by combusting extracted soil samples as described earlier.

C. Reported Results:

The mobility of DPX-L5300 in the different soils was as follows:

Fargo Silty Clay Soil Column:

DPX-L5300 leached readily through Fargo silty loam. The radioactive material applied to the Fargo soil was eluted primarily as DPX-L5300 (71%) with 28% of the eluate accounted for as the acid sulfonamide while saccharin and sulfonamide, the other decomposition products, were not present in the eluate sample. Saccharin was present in the soil extract.

Gardena Soil Column:

DPX-L5300 leached readily through Gardena soil. The applied radioactivity was slightly retained on the Gardena column and 83% of the material in the eluate was present as DPX-L5300. Analysis of the 0-4" sections of the soil revealed that acid sulfonamide and saccharin accounted for more than 95% of the extractable radioactivity and it indicated that almost all the DPX-L5300 that remained on the column decomposed.

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Sassafras Soil Column:

DPX-L5300 leached readily through Sassafras loamy sand and accounted for 67% of the applied radioactivity. The remaining radioactivity was distributed between saccharin, acid sulfonamide and sulfonamide.

Keyport Soil Column:

DPX-L5300 behaved distinctly different on Keyport soil than on Gardena, Sassafras and Fargo soils, degraded considerably on the Keyport soil and accounted for only 8% of the eluted radioactivity. The top section (0-2") contained 7% of the applied radioactivity and even smaller quantities of radioactive material were present in the other sections. The soil extracts from the top segment (1) contained 69% DPX-L5300, 24% saccharin and 7% sulfonamide. Section 6 extract contained 71% saccharin and 29% DPX-L5300. Most of the radioactive material recovered from aged Keyport soil was sulfonamide, saccharin and acid sulfonamide (98%) and only traces of DPX-L5300 were present.

D. Study Author's Conclusions:

DPX-L5300 will have high mobility through Sassafras loamy sand, Gardena silt loam and Fargo silty clay (K_d <0.2). DPX-L5300 decomposed readily on the Keyport soil column and its degradates were eluted readily through the soil.

E. Reviewer's Discussion and Interpretation of Results:

The leaching experiment appeared to provide valid scientific results and the reviewer did not find a cause to question the results or disagree with the author's stated conclusions.

10.5 A. Study Identification: Octanol/Water Partition Coefficient of [Phenyl-^{14}C(U)] DPX-L5300.

The study was conducted by H. Y. Mohammed of the Agricultural Chemical Department, Research Division Experimental Station of Du Pont (Document No. AMR-407-85).

B. Material and Methods:

One ml of a 1060 ppm solution of radiolabeled [phenyl-^{14}C(U)] DPX-L5300 with specific activity of 20.5 microCi/mg and radiochemical purity of 97% was pipetted into three separate 50 ml centrifuge tubes, the solvent was evaporated under a stream of nitrogen and the residue was redissolved in 10 ml of n-octanol to give a 106 ppm solution. Then, 10 ml of a pH 7, 0.005 M NaH_2PO_4 buffer and the closed tubes were shaken for 15 minutes and then centrifuged for 5 minutes at 2500 rpm to facilitate separation. A volume of 100 microliters of both the octanol and the aqueous phase were drawn and analyzed by LSC. The octanol phase was separated and discarded and fresh 10 ml of octanol added. The extraction procedure was repeated three times.

C. Reported Results:

The octanol/water partition coefficient was determined from the three trials at 0.3± 0.03 and comparable values were obtained in consecutive extractions indicating that partitioning was independent of the concentration in the range used for this experimentation.

D. Study Author's Conclusions:

No additional conclusions to those stated in the results section.

E. Reviewer's Discussion and Interpretation of Study Results:

The reviewer did not find a cause to question the stated results.

11. COMPLETION OF ONE LINER:

Not completed.

12. CBI APPENDIX:

Attachment.

EXPRESS 128887

Page _____ is not included in this copy.

Pages 11 through 29 are not included in this copy.

The material not included contains the following type of information:

_____ Identity of product inert ingredients.

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