128901

Date Out EFB:

SEP 09 1985

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

From: Samuel M. Creeger, Chief
Review Section No. 1
Exposure Assessment Branch
Hazard Evaluation Division (TS-769)

Attached please find the environmental fate review of:

Reg./File No.: 352-UGA

Chemical: DPX-F6025

Type Product: Herbicide

Product Name: Classic™ Herbicide

Company Name: du Pont

Submission Purpose: New Herbicide for Use on Soybeans

ACTION CODE: 110

Date In: 2/15/85

EAB # 5302

Date Completed: 5/13/85

TAIS (level II)	Days
31	13

Deferrals To:

_____ Ecological Effects Branch

_____ Residue Chemistry Branch

_____ Toxicology Branch

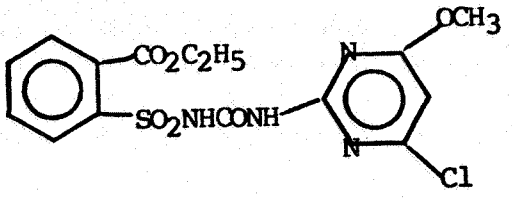
1.a CHEMICAL:

Ethyl 2-[[[(4-chloro-6-methoxypyrimidin-2-yl)amino]carbonyl]amino] sulfonyl]benzoate.

Benzoic acid, 2-[[[(4-chloro-6-methoxy-2-pyrimidinyl)amino]carbonyl] amino]sulfonyl]-, ethyl ester

DPX-F6025

INF-6025



1.b Physical Properties:

Molecular Weight: 414.8
Melting Point: 181°C
Solubility in Water: 1200 ppm at 25°C at pH 7
Vapor Pressure at 25°C: 1.5×10^{-5} mm Hg
Octanol/Water Partition Coefficient: 1.3

2. TEST MATERIAL:

^{14}C-(2-Pyrimidine)-DPX-F6025

^{14}C-(Phenyl(U))-DPX-F6025

3. STUDY/ACTION TYPE:

Application for an Experimental Use of DPX-F6025 in or on Soybeans as an Herbicide (du Pont Classic™ Herbicide).

C. STUDY IDENTIFICATION:

- Photodegradation of ^{14}C-DPX-F6025 on Soil
- Aerobic Soil Metabolism of ^{14}C-DPX-F6025
- Crop Rotation Study with ^{14}C-DPX-F6025 in the Greenhouse
- Batch Equilibrium (Adsorption/Desorption) and Soil Thin Layer Chromatography Studies with DPX-F6025 [Phenyl-^{14}C]
- Octanol/Water Partition Coefficient of DPX-F6025 Soybean Herbicide Candidate.

5. REVIEWED BY:

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

Abramovitch
SEP 09 1985
Date: / /85

6. APPROVED BY:

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

Samuel Creeger
SEP 09 1985
Date: / /85

7. CONCLUSIONS:

Hydrolysis

The hydrolysis study was reviewed and found satifactory in the EAB report of January 10, 1984. DPX-F6025 did not undergo any noticeable hydrolysis at pH 7 and 9 at 25°C. At pH 5 at 25°C, DPX-F6025 hydrolyzed with half lives ranging from 15.6 to 20.6 days. The two hydrolysis products at pH 5 were ethyl 2-(aminosulfonyl)benzoate and 4-chloro-6-methoxy-2-pyrimidinamine.

Temperature (°C)	pH	Half Life (day) 5	7	9
25		15.6-20.6 (a)	(a)	

(a) no noticeable hydrolysis

Fish Accumulation

Not submitted and a waiver was requested based on the reported octanol/water partition coefficient of 1.3 and information showing the hydrolysis products of DPX-F6025 to have even lower $K_{o/w}$. Since correlation between octanol/water partitioning and fish accumulation is only accurate within a factor of 100, our position will be that DPX-F6025 and its degradation products have potential to accumulate in fish to levels 130 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.

Water/Octanol Partitioning Coefficient

The study appeared to produce valid results determining the octanol/water partition coefficient for DPX-F6025 as 1.3. The degradation products of DPX-F6025 from hydrolysis were found to have even lower solubility in octanol than the parent compound.

Photodegradation on Soil

The photodegradation study did not satisfy the EAB data requirement. The range and intensity of the light was not reported as comparable to sunlight (and should have been). In addition, it was not clear what

fraction of the radiolabeled material applied to the soil was exposed to radiation. DPX-F6025 did not undergo photolytic degradation when exposed to UV light.

Aerobic Soil Metabolism

The aerobic soil metabolism study appeared to provide valid results and satisfied the data requirements for registration. DPX-F6025 underwent initial degradation to ethyl 2-aminosulfonylbenzoate and 4-chloro-6-methoxy-2-pyrimidine amine with a half life of 7.5 weeks. The initial degradates did not undergo significant degradation in the following 52 weeks and identical behavior was observed in sterile and non-sterile soils. Demethylated DPX-F6025 was reported in only 4.4-13.2% between 24 and 52 weeks.

Crop Rotation

The crop rotation study was found questionable and some of the experimental procedures (such as the extraction procedures) used in the study should be reexamined. A higher percentage of demethylated DPX-F6025 was observed in the soil of the crop rotation study than in the soil metabolism study.

Batch Equilibrium and Soil TLC

The study provided results to complement the pending submission of the leaching and the field dissipation studies.

8. RECOMMENDATIONS:

The registrant should be made aware of the following comments with regard to the proposed use on soybeans. Other data requirements to support the proposed use of DPX-F6025 on soybeans are addressed in the other evaluation for this use dated 9/9/85.

Hydrolysis- the requirement was satisfied in a previous EAB review (Jan. 10, 1984).

Soil Photolysis-The study was not acceptable (see comments in section 10.4.E).

Rotational Crop Rotation-The study was not acceptable (see comments in section 10.5 E).

Fish Accumulation- The requirement has been waived. However, see comment in section 7 and the review of the octanol/water partitioning study reviewed in section 10.1.

Leaching- The requirement has been satisfied. However see section 10.3.E for comments.

Aerobic Soil Metabolism- The data requirement is considered unfilled pending reconciliation between it and the results of the analysis of the soil used in in the rotational crop data.

9. BACKGROUND:

A. Introduction: An experimental use permit (352-EUP-113) and a temporary tolerance on soybeans (PP3G2959) were approved by EPA

on May 9, 1984. Du Pont is seeking to register DPX-F6025 as an Herbicide for use in or on Soybeans. They would like to market du Pont Classic™ Herbicide nationwide. (refer to another review dated September 9, 1985).

B. Directions for Use:

"Classic" Herbicide contains 25% of DPX-F6025 as the active ingredient(75% inert ingredients). It should be thoroughly mixed with water in a spray tank before adding any other material and used within 24 hours of mixing. Applications of 0.5-1.0 oz of the herbicide, dissolved in about 10 gallons of water was recommended per acre (a maximum use of 1.0 oz per crop per acre).

10 DISCUSSION OF INDIVIDUAL TESTS OR STUDIES:

10.1 A. Study Identification: Octanol/Water Partition Coefficient of DPX-F6025.

The study was done by the Biochemicals Department, Research Division Experimental Station, Wilmington, Delaware(Report No. AMR-142-83).

B. Material and Methods:

A one ml acetonitrile solution of 14C-phenyl-DPX-F6025 (997 ppm) was pipetted into three 40-ml centrifuge tubes and the solvent was evaporated under a flow of nitrogen. The residue was redissolved in 10.0 ml of pH 7 buffer solution giving a 100 ppm solution. Then, 10 ml of octanol was added to each tube, the tubes were capped, shaken vigorously for ten minutes in a 25°C bath, and centrifuged to facilitate phase separation. The water and octanol layers were analyzed separately by TLC to determine whether any decomposition of DPX-F6025 occurred during the partitioning. Aliquots of the retained water and octanol were analyzed by LSC for total 14C concentration.

C. Reported Results:

The K_{ow} of DPX-F6025 was determined as 1.3 ± 0.2. The octanol phase appeared to contain only the parent compound. On the other hand, the water fraction contained three minor decomposition products, none of which identified as the major hydrolysis product of DPX-F6025, and were apparently more polar than the parent compound.

D. Study Author's Conclusions:

The DPX-F6025 partitioning coefficient between octanol and water was determined as 1.3, placing it in a category of compounds having a low bioaccumulation potential. In addition, the octanol phase did not contain any other degradation product (including the hydrolysis product), indicating that they too are not likely to bioaccumulate.

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

The study appeared to have provided valid results using dilute solutions of radiolabeled DPX-F6025. Based on the results DPX-F6025 has $K_{o/w}$ of 1.3.

10.2 A. Study Identification: Aerobic Soil Metabolism of ^{14}C DPX-F6025

The study was conducted by the Agricultural Chemicals Division of Du Pont, Research Division Experimental Station, Wilmington, Delaware by P. T. Hardesty (Document No. AMR-138-83).

B. Materials and Methods:

To biometer flasks containing 50 gm of sterilized and non-sterilized Flanagen silt loam and Woodstown sandy loam (characteristics of soils attached to the report) was added 250 microliters of a methylene chloride solution of DPX-F6025 (0.02 gm/liter) to give a soil concentration of 0.1 ppm of [^{14}C-phenyl]-DPX-F6025 or 0.1 ppm [^{14}C-pyrimidine]-DPX-F6025. After the solvent evaporated, water was added to bring the moisture level to about 75% of capacity. Then, 10 milliliters of 0.1N NaOH was added to each biometer ($^{14}CO_2$ trap?). Each flask was sealed with a rubber stopper and incubated in the dark for 52 weeks at 25°C. The application rate in all studies was equivalent to 1.4 oz of the active ingredient per acre. Identical soils were treated with an aqueous suspension of ^{14}C-cellulose to confirm the viability of the microorganisms. The entire 10 ml NaOH solution from each flask was periodically removed and replaced with fresh 10 ml aliquots of 0.1 N NaOH. Aliquots from the NaOH solutions were analyzed for radioactivity by LSC. Soil samples of 50 gm were taken at specified time intervals and extracted with three successive 100 ml portions of $CH_2Cl_2/CH_3OH/2M\ (NH_4)_2CO_3$ (3/4/1 by volume). Other samples were extracted with three successive 150 ml portions of $CH_2Cl_2/CH_3OH/HCOOH$ (75/25/1 by volume). Aliquots from each extraction were analyzed for total radioactivity by LSC. Other aliquots were concentrated under vaccuum (at <40°C), and analyzed by TLC. Further cleanup was achieved by extracting the methylene chloride solution with an aqueous phosphoric acid (pH 2). Some concentrated extracts were chromatographed by HPLC and the radioactive peaks were separated and collected for future chromatographic and mass spectral analysis.

C. Reported Results:

The degradation half-life in each soil was about 7.5 weeks. After 24 weeks, between 19.1-25.6% of the DPX-F6025 remained intact. The major ^{14}C degradation product in both soils from pyrimidine-labeled DPX-F6025 was ^{14}C-4-chloro-6-methoxy-2-pyrimidine amine; 44.5% in Flanagen silt loam soil and 29.5% in Woodstown sandy loam soil. The major degradation product of phenyl labeled DPX-F6025 was ^{14}C-2-aminosulfonylbenzoic acid; 60.1% in the Flanagen soil and 36.8% in the Woodstown soil. Within 52 weeks 5-10% of the ^{14}C was evolved as $^{14}CO_2$ and 5% of the DPX-F6025 remained intact. Demethylated DPX-F6025 was reported present in 4.4, 4.6, 4.4 and 18.6% in the two studied soils with the two radiolabeled materials (assuming the 18.6% value is in error, a 4.4-4.6% value obtained). Extractions with MMF (methylene chloride/ methanol/formic acid 75/25/1) removed 23-49% of the ^{14}C. In a separate study, a soil sample that was incubated in the dark was extracted with MMF and then with 0.1N NaOH. The NaOH extraction removed an additional 64 and 44% from the Flanagan and Woodstown soils, respectively, and a final extraction with an 0.1N HCL solution removed only 3-4% of the ^{14}C and was not analyzed.

In conclusion, 91.3%-96% of the radioactivity was removed by extraction and the major degradation products were identical to those obtained via hydrolysis. The identity of the degradates were identified by co-chromatography with authentic reference standards on HPLC and by mass spectral analysis (an error is the structure posted in Figure 9-top). The study accounted for the fate of more than 95% of the applied radioactivity though not all the degradates were identified.

D. Study Author's Conclusions:

The author concluded that the DPX-F6025 underwent aerobic soil degradation in non-sterilized Flanagen silt loam and Woodstown sandy loam soils mainly via the hydrolysis route with half lives of 7.5 weeks. There was little difference between the degradation in sterile and non-sterile soils indicating that microbial degradation was not an important degradation pathway. After 52 weeks, microbial degradation generated only 5-10% of the applied ^{14}C as $^{14}CO_2$ while the other ^{14}C degradates were ^{14}C-ethyl 2-aminosulfonylbenzoate and ^{14}C-4-chloro-6-methoxy-2-pyrimidine amine. The soils were demonstrated to be microbially active.

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

The study was able to trace over 95% of the initially applied radioactivity throughout the study and generally appeared to provide valid scientific results. The initial degradation of DPX-F6025 proceeded with a half life of 7.5 weeks to form major degradates that were identical to those obtained via hydrolysis. According to the author "the results suggest that chemical hydrolysis is the major degradative pathway for DPX-F6025 under these conditions." Demethylated DPX-F6025 was reported after 24 weeks at about 4.6%, 5.3-13.2% after 52 weeks. On the other hand, demethylated DPX-F6025 was reported present between 44.7-45.5% at weeks 34-41 of the crop rotation study. After 52 weeks only 5-10% degraded to CO_2. The degradation products distribution appeared inconsistent between the reported soil degradation study and the crop rotation study but might be due to a higher microbial activity in the crop rotation study.

10.3 A. Study Identification: Batch Equilibrium (Adsorption/Desorption) and Soil Thin Layer Chromatography Studies with DPX-F6025 [Phenyl-^{14}C].

The study was conducted by Thomas M. Priester at the Agricultural Chemical Department, Research Division Experimental Station of Du Pont (AMR-198-84).

B. Material and Methods:

A [^{14}C Phenyl] DPX-F6025 was applied to four different soils (Cecil sandy loam, Flanagan silt loam, Keyport silt loam and Woodstown sandy loam-see attachment for soil characteristics) in aqueous solutions of 0.01M $CaSO_4$. The concentrations of the various stock solutions were 0.2, 0.5, 1.0, 2.5 and 6.0 (The solubility of DPX-F6025 in water was reported to be approximately 1200 ppm at pH 7 and 25°C (AMR-137-83)). The radiolabeled DPX-F6025 was applied in 20 ml fractions to 20 gm portions of an oven dried soil, mixed for 24 hr at 25°C and then centrifuged for 10 minutes at 2000 rpm. The clear supernatant solution was then removed and aliquots were

taken and analyzed by LSC to determine the radioactive content. After discarding a known volume of the supernatant, the appropriate volume of 0.01M $CaSO_4$ solution was added to reestablish the original total weight and 1:1 (w:w) soil to water ratio. The procedure was repeated five more times (24 hr, 25°C). The aqueous extracts containing DPX-F6025 were acidified to pH 3.2 and extracted 3 times with methylene chloride. The combined methylene chloride extracts were concentrated on a rotary evaporator at 40°C to approximately 2 ml and co-chromatographed on a silica TLC plate with DPX-F6025 and their potential degradates and quantified on a TLC analyzer. In the adsorption studies the concentration of radioactive material adsorbed onto the soil after equilibrium (C_s) was determined by subtracting the concentration in the aqueous solution at equilibrium (C_2) from the concentration in the standard solution (C_1). The C_2 and C_s values were plotted on log-log paper to generate the Freundlich isoterms. The adsorption distribution constant (K_a) of each compound on each soil was calculated as the C_s value corresponding to a C_2 value of 1 ppm. Coefficient of adsorption per unit of organic matter were calculated from each K_a values using the equation:

$$K_{a,\,OM} = \frac{K_a(100\%)}{(\%\ OM \text{ in soil})}$$

The mobility of DPX-F6025 was also studied by soil TLC. Each soil was coated as a 400 micrometer layer onto a 20 x 20 cm thin glass. One microliter aliquots of the sample and reference standard solutions (1 mg compound/ml) were spotted 3 cm from the bottom of the plate. The bottom 0.5 cm of the plate was then submerged in water and the water was allowed to ascend to a height of 10 cm. The plates were then air dried for 24 hr and exposed to X-ray film for two weeks.

C. Reported Results:

DPX-F6025 was very weakly adsorbed (K_a = 0.2-0.4) on the two sandy loam soils and only weakly adsorbed (K_a = 3-7) on the two silt loam soils. Adsorbed radioactivity was readily desorbed from the sandy loam soils but more tightly retained on the silt loams. DPX-F6025 had low mobility on Keyport silt loam (R_f=0.18), intermediate mobility on Flanagan silt loam R_f=o.41) and Cecil sandy loam (R_f=0.59) and high mobility on Woodstown sandy loam (R_f=0.71).

D. Study author's Conclusions

The study author concluded that the ease of desorption and mobility was inversly proportional to the % of organic matter in the soils.

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

A concern has been raised over potential hydrolysis at pH 3.2 during the work up (the hydrolysis data showed increased hydrolysis with decreased pH). The active ingredient has potential to leach in sandy soils of low organic matter content.

10.4 A. Study Identification: Photodegradation ^{14}C DPX-F6025 on Soil.

The study was done at the Agricultural Chemical Department, Research Division Experimental Station of Du Pont at Wilmington, Delaware by P. T. Hardesty (Document No. AMR-192-84).

B. Materials and Methods:

Identical ^{14}C-labeled Chemicals to those listed in sections 10.2 and 10.3 were applied to the non-sterilized soils listed in 10.3 at a rate of 0.1 ppm (or 1.4 oz/acre). The soils were exposed for one month under a bank of 6 fluorescent black photolysis lamps alternating with 6 fluorescent sun lamps, having a photolysis radiant energy in the 300-800 nm range. The average temperature under the light was 38°C. Similarly treated samples were kept in the dark to serve as controls. Extractions of the ^{14}C Material from the soils was done with 97% efficiency with identical solvents to those used in the soil degradation studies. The identity of the extracted products was determined as in section 10.3 by co-chromatography with authentic samples.

C. Reported Results:

The parent compound degraded on both photolytically exposed and non-exposed soils with identical half lives of 0.7-1.1 weeks to identical degradates to those formed via hydrolysis and/or soil metabolism (sections 10.1, 10.3).

D. Study Author's Conclusions:

The author's study concluded that the obtained results generally paralleled those obtained in the aerobic soil metabolism study and indicated that photolysis was not an important degradative pathway for DPX-F6025. The slightly faster degradation rate was probably due to the slightly higher temperature in which the photolysis was conducted (38 versus 25°C).

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

The light source used in the study is not acceptable since it had most of its emission in the UV range and was not shown to be comparable to that of natural sunlight. In addition, the study did not specify how the material was applied and what percentage was exposed (was the soil spread out on a glass plate?).

10.5 A. Study Identification: Crop Rotation Study with ^{14}C-DPX-F6025 in the Greenhouse.

The study was conducted by M. K. Koeppe and B. C. Rhodes at the identical location where the previous studies were conducted (document No. AMR-268-84).

B. Material and Methods:

A sandy loam soil was treated with [^{14}C-phenyl(U)] DPX-F6025 at the rate of 0.6 oz a.i./A and aged for 120 days in the greenhouse. Barley, beets, cotton and peanuts were planted after the 120-day aging period and grown to maturity. Plastic saucers were used to prevent escape of radioactivity from the test system. Crop samples were harvested and analyzed at various stages of growth and at maturity. Soil samples were removed from each pot to the depth of six inches using a Hoffer tube at planting time and at time of crop maturity. Triplicate 2-3 gm aliquots of each air-dried pulverized soils were combusted in a sample oxidizer and the ^{14}C was trapped and quantitated by LSC. Other soil samples were extracted with MMF

(methylene chloride: methanol:formic acid 75:25:1). Aliquots of mature plant tissues were placed in 250 ml centrifuge bottles, along with 130 ml of acetone:water(70:30,v:v) extraction solvent and macerated. The extraction solvent was analyzed by LSC to determine the total ^{14}C material extracted. Then, "acetone was evaporated from the composite acetone:water extracts using a rotatory evaporator at 37°C. The pH of the remaining aqueous was adjusted to 8.5-9.5 using 12.5 N NaOH to ionize the DPX-F6025 and/or metabolites". The aqueous solution was then extracted with hexane (no radioactivity in the hexane), acidified to pH 2.5 with 85% phosphoric acid ("to protonate the DPX-F6025 and/or metabolites"), and then extracted with methylene chloride and analyzed by LSC.

C. Reported Results:

At final harvest, barley straw and peanut and cotton foliage, contained total ^{14}C residues of 0.025, 0.016 and 0.016 ppm, respectively, but contained very low concentrations (<0.005 ppm) of DPX-F6025 and its major metabolites. Total ^{14}C-residue concentration in each of the other mature crop fractions were insignificant(<0.01). ^{14}C residue levels in the soil samples declined from 0.019 ppm at treatment to 0.0022 ppm at the final crop harvest. Benzoic acid, 2-[[4-chloro-6-hydroxypyrimidine-2-yl) aminocarbonyl]aminosulfonyl]-, ethyl ester represented about 45% of the total applied radioactivity in soils collected at final harvest. Intact DPX-F6025 accounted for 5-8% of the total radioactivity in these soils while unextracted (bound) material accounted for 32-34%.

D. Study Author's Conclusions:

Total ^{14}C residue concentration in each of the mature crop fractions were insignificant(<0.01 ppm).

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

The reviewer is seeking clarifications for some of the experimental procedures and results.

The soil residue analysis presented in this study indicated that 45-46% of the radioactivity corresponded to a degradation product resulting from demethylation of DPX-F6025 and 5-8% of the radioactivity represented intact DPX-F6025. Products resulting from hydrolysis of either DPX-F6025 or its demethylation product were not identified in this study. On the other hand, the soil metabolism study presented in section 10.3 concluded that chemical hydrolysis was the major degradation pathway. (Why was demethylated DPX-F6025 formed in this soil and not in the aerobic soil metabolism study?). Also, during the work up procedure the aqueous solution was acidified to pH 3.2 with phosphoric acid (more acidic than in other studies). The hydrolysis data indicated that DPX-F6025 rate of hydrolysis increases with decreasing pH (15.6 days at pH 5 at 20°C) and yet no hydrolysis was reported. The extraction solvent used to extract DPX-F6025 and its degradation products from soils was MMF for both the crop rotation study and the soil degradation study, but was not the solvent of choice for extractions from plants. Instead, a

mixture of acetone water was used (70:30, v:v). According to the procedure, the acetone was evaporated prior to adjustment of the pH to 8.5-9.5 with 12.5 N NaOH (Why was such concentrated solution (50%) of NaOH used?). In using that procedure, potential traces of acetone (forms an azeotrope with water) were likely to remain and react with NaOH (to form condensation products). Can the reviewer be assured that these potential complications did not affect the results?). In general, due to the questionable work up procedures used in the crop rotation studies, the reviewer has various doubts about the validity of the results.

11. COMPLETION OF ONE LINER:

Not completed.

12. CBI APENDIX:

None

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