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: Registration on Soybeans

ACTION CODE: 111

Date In: 6/12/85

EAB # 5670

Date Completed: SEP 09 1985

| TAIS (level II) | Days |
|---|---|
| 31 | 12 |

Deferrals To:

_____ Ecological Effects Branch

_____ Residue Chemistry Branch

_____ Toxicology Branch

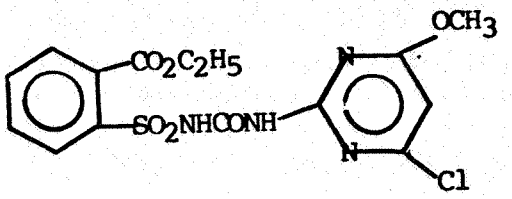
① +2

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




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: $1.5 \times 10^{-5}$ mm Hg
Octanol/Water Partition Coefficient: 1.3

2. TEST MATERIAL:

33.3 micro Ci/mg and 96.6-98.0% radiochemical purity $^{14}C$-(2-Pyrimidine)-DPX-F6025

58.5 micro Ci/mg and 97.6-99.9% radiochemical purity $^{14}C$-(Phenyl(U))-DPX-F6025

3. STUDY/ACTION TYPE:

Additional data in support of registration of DPX-F6025 for use in Soybeans as an Herbicide (du Pont Classic™ Herbicide).

4. STUDY IDENTIFICATION: Accession No. 258060

- Soil Column Leaching Behavior of [Phenyl-$^{14}C$(U)]DPX-F6025.
- Terrestrial Dissipation of $^{14}C$-Labeled DPX-F6025.
- Aqueous Photolysis of $^{14}C$-Labeled DPX-F6025.
- Anaerobic Aquatic Metabolism of $^{14}C$-Labeled DPX-F6025.

5. REVIEWED BY:

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

Abramovitch

Date: / /85

SEP 09 1985

2

13

6. APPROVED BY:

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

SEP 09 1985

Date: / /85

7. CONCLUSIONS:

Soil Column Leaching Behavior:

The study appeared to provide valid scientific results indicating that DPX-F6025 has high potential to leach into the ground water. The primary degradates were identified but not their degradation products although they were reported to have even a greater potential to leach into the soil than their precursors. Fulfillment of data requirement is pending the determination of the identity of the major secondary degradates.

Terrestrial Dissipation:

The terrestrial dissipation study did not provide a good account for the total DPX-F6025 material balance. In addition, it did not seek information about potential leaching to depths of more than 32 cm although the results of the study and those obtained in the soil column leaching study indicated that DPX-F6025 and its degradates were likely to leach in various soils. In the absence of further information, the review must conclude that DPX-F6025 has the potential to leach and contaminate ground water although at very low concentrations when used as proposed. Since it was not clearly demonstrated that DPX-F6025 cannot be detected immediately after application in a standard field dissipation study due to the very low application rate, we must assume that a standard field dissipation study (without cylinders) can be used.

Anaerobic Aquatic Metabolism:

The anaerobic aquatic metabolism study appeared to provide good scientific data to satisfy the requirement for either anaerobic soil or anaerobic aquatic data. DPX-F6025 underwent anaerobic soil degradation by hydrolysis and microbial degradation with half lives of 2-6 weeks in the Florida and the Pennsylvania studies. Hydrolysis resulted in sulfonamide and pyrimidine amine and microbial degradation in demethylated DPX-F6025. Surprisingly, the anaerobic degradation resulted in more microbial degradation and less hydrolytic degradation than observed in the soil degradation study.

Aqueous Photolysis:

The study did not satisfy the EAB data requirement and additional modification and clarifications for the study were requested as cited in section 10.4.E. The study author concluded that the photodegradation of DPX-F6025 in sterilized buffers of pH's 5, 7 and 9 proceeded fast with a half life of 2 days to form rearrangement products. On the other hand, hydrolytic degradation in the dark proceeded much slower with half lives of 18-30 days to form different products (hydrolysis products).

Conclusions of reported studies from previous submissions:

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 which complement the leaching and the field dissipation studies reviewed in this evaluation.

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 other evaluation for this use dated 9/9/85.

Soil Column Leaching-Data show DPX-F6025 to have high potential for leaching. The leaching data requirement will be satisfied when the polar degradation products are identified.

Field (Terrestrial) Dissipation- This study was conducted without using the standard protocol. In order to have the modified study accepted by the EAB, the registrant is encouraged to demonstrate that conducting a typical field dissipation study at the maximum application rate, will not enable them to obtain usefull information due to the low application rate. This data requirement is not satisfied pending further resolution of this issue.

Anaerobic Aquatic Metabolism- The data submitted satisfies the requirement for anaerobic soil or anaerobic aquatic metabolism data.

Aqueous Photolysis- The data requirement is not satisfied. Refer to section 10.4 E.

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 in 1985. Additional data was submitted with this report (see previous reviews and another 9/9/85 review).

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 product, 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: Soil Column Leaching Behavior of [Phenyl-$^{14}$C(U)] DPX-F6025.

The study was conducted by A. C. Barefoot of the Agricultural Chemicals Department, Research Division Experimental Station of DuPont (Document No. AMR-306-84).

B. Materials and Methods:

Flanagan silt loam, Cecil sandy loam, Keyport silt loam and Woodstown sandy loam soils, sieved between 9-30 mesh (see attached characteristics) were packed to a height of 12-13 inches in separate 2 inch diameter glass tubes containing 8 inches of water. Excess water was allowed to drain out and [Phenyl-$^{14}$C(U)] DPX-F6025 (0.03 mg, 1.16 microCi/mg) was applied in 1 ml acetonitrile/water (60:40) solution and the column was covered with a layer of sand. A 4-inch head of water was then added to the column until a 1 liter reservoir was consumed. That was equivalent to about 20 inches of water. Aliquots collected were examined by LSC for total radioactivity and selected samples were co-chromatographed on HPLC with authentic samples of DPX-F6025 and the potential degradates seen in the soil degradation study. The amount of radioactivity in each 2 inch soil column fraction starting from the top was determined by quantitating the evolved $^{14}CO_2$ from combustion. Soil samples were also extracted with 0.1M ammonium carbonate and then by MMF (methylene chloride: methanol:formic acid 75:25:1). The extracts were made miscible by addition of methanol, filtered, concentrated, and analyzed by LSC and HPLC. Unextracted residues were determined by combusting weighted extracted soils as described earlier.

C. Reported Results:

More than 95% of the applied radioactivity was eluted from the Cecil and the Woodstown column and DPX-F6025 accounted for 92% of the radioactivity in the eluate. DPX-F6025 was slightly retained on the Flanagan column. Analysis of the eluate showed that 92% of the radioactivity in the eluate was DPX-F6025. Analysis of the soil from the Flanagan column (8-12 inches) indicated that DPX-F6025 (51-55%) and sulfonamide (28-34%) accounted for most of the radioactivity. In distinct contrast to its behavior on Woodstown and Cecil columns, DPX-F6025 was not eluted from the Keyport column and only 5% of the applied radioactivity was found in the eluate of which only 3% was DPX-F6025 (0.15% of the applied DPX-F6025). The top section (0-2 inches) of the Keyport column contained 36% of the applied radioactivity and the following sections contained decreasing amounts of radioactive material. In the top soil, DPX-F6025 and sulfonamide accounted for 93% of the extracted radioactive material.

D. Study Author's Conclusions:

DPX-F6025 leached readily through Woodstown sandy loam and Cecil sandy loam. DPX-F6025 leached to a lesser degree through Flanagan silt loam and only slightly through Keyport soil. These results were consistent with the results obtained in the adsorption/desorption experiments. The degradates obtained from the Flanagan silt loam soil were identical to those obtained in the aerobic soil metabolism studies and were eluted even faster than the parent compound.

E. Reviewer's Discussion and Interpretation of Results:

The leaching experiment appeared to provide valid scientific results indicating that both DPX-F6025 and its degradates are likely to leach. The experiment provided a quantitative account for the $^{14}C$ material. Unfortunately, the polar degradates (59.4% in the Flanagan aged soil and 99% in the Keyport soil) were not identified. These degradates are likely to leach into soils (even more than the parent compound) and contaminate the ground water and therefore should be identified (particularly, the major ones).

10.2 A. Study Identification: Terrestrial Dissipation of $^{14}C$ Labeled DPX-F6025

The study was conducted by E. M. Venzon and P. T. Hardesty at the Agricultural Chemical Department, Research Division Experimental Station of Du Pont (document No. AMR-352-85).

B. Materials and Methods.

Stainless steel cylinders (15" long x 3 7/8 i.d.) were driven into soils (charatersitics of soils attached to the report) cleared of vegetation at four sites leaving a 1" rim above the ground to minimize runoff. The soils in each cylinder were treated with 100 microliters of the acetone solution of the radiolabeled material (the concentration of the solution was determined by LSC to measure the application rate at 2 oz/acre), followed by 50 ml of water (to simulate 0.6 inches of rainfall). Water was added peridically to simulate rainfall through out the study period as shown by the attached data. Cylinders were withdrawn at each site at approximate intervals of 0, 2, 4, 8, 16, 26, 52 and 78 weeks after treatment and frozen until analysis. For analysis, the soil from each cylinder was removed and divided into 4 segments (of 5 cm each) begining at the soil surface. Each segment was air dried and homogenized and 5 gm samples were combusted and the evolved $^{14}CO_2$ was quantitated in order to determine the total amount of radioactive organic material in the sample. Soil segments that were found to contain more than 10% of the applied radioactivity (or more than 0.01 ppm of $^{14}C$-DPX-F6025 equivalent) were further analyzed for degradates. These samples (50 gm each) were centrifuged over night at 5°C with 40 ml of 0.1M ammonium carbonate and then extracted with with 3x150 ml of methylene chloride/methanol/formic acid (MMF, 75/25/1 by volume). The combined extracts were diluted with 100 ml of methanol (to dissolve the two layers), filtered, and aliquots were analyzed by LSC for the total radioactivity. The extraction fraction was then concentrated (most of the organic solvents distilled off). The aqueous residue was adjusted to pH 9 with the ammonium carbonate solution and stored overnight. The precipitate

formed was later found to contain less than 1% of the radioactivity and was not analyzed further. Under the above extraction procedure, 98% of a tested DPX-F6025 remained intact. The extracted material was analyzed by HPLC and by TLC along with DPX-F6025 and its degradation products.

C. Reported Results:

The terrestrial dissipation of DPX-F6025 was studied for 78 weeks. The results indicated that the radiolabeled DPX-F6025 had a half life of 1-6 weeks at the four soils studied, with the 6 week half life observed in the high ion exchange capacity and high organic content soil. The DPX-F6025 decomposed by hydrolysis to ethyl 2[[amino]sulfonyl]benzoate and 4-chloro-6-methoxypyrimidine-2-yl) amine or by demethylation to demethyl DPX-F6025. The results for the following soils were as follows: The Delaware soil; 95-100% of the radioactivity was accounted for immediately after application at some time intervals: The total radioactivity balances reported for the four soils was at week 0, when [phenyl-$^{14}$C] DPX-F6025 was used, were 101.6% for the Delaware soil, 92.7% for the Illinois soil, 92.5% for the Mississippi soil and 105.5% for the North Carolina soil. After 4 weeks, these values changed to 48.7%, 75.2%, 38.1% and 54.2% for the Delaware, Illinois, Mississippi and North Carolina soils respectively. After 78 weeks these values changed to 27.6%, 50%, 22.7% and 10%, respectively. These values include the total amount of radioactive material found in the four fractions to the total depth of 32 cm.

D. Study Author's Conclusions:

The study author concluded the results show little vertical movement of the radio active material (either DPX-F6025 and its major metabolites) with less than 4% of the applied radioactivity at deeper than 20 cm below the soil surface. DPX-F6025 and its metabolites exhibited significant mobility only in soil with a high (78%) sand content. These results, the author concluded, were in good agreement with the results obtained in the soil column leaching and the adsorption/desorption studies. The results observed in the field studies also have reaffirmed the results obtained in the aerobic soil studies placing hydrolysis as a major degradation pathway for DPX-F6025. The author cited that the total amount of recovered radioactive material remained high during the initial 8 weeks of the study (May and June). During the hot months of July and August there was a significant amount of radioactivity loss (probably due to loss of $^{14}CO_2$) and a much lower loss of radioactivity during the following 4 months. The results obtained from the Delaware, Illinois, North Carolina and Mississippi soil cylinders showed a similar pattern.

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

The data reviewed gave a poor account for the total amount of the applied radioactivity. DPX-F6025 was reported to leach only moderately through the Flanagan silt loam (reported to leach readily through Woodstown sandy loam and Cecil sandy loam) and 50% of the radioactivity was accounted for after 78 weeks. Soil degradation studies reported earlier in Flanagan silt and Woodstown sandy loam soils was able to trace 95% of the radioactivity (69.7% in this study) and only 5-10% loss was attributed to loss of $^{14}CO_2$. On the other hand, the studies conducted in the North Carolina

and Mississippi sandy soils accounted for only 23.4% and 33.1% of the applied radioactivity after 52 weeks. Interestingly, the North Carolina soil has a 78% sand content and DPX-F6025 was reported to leach readily in such soils in the soil column leaching study report. The Mississippi soil has only 8% sand and 74% silt but is similar to the North Carolina soil in having a low organic content (1.4 and 1.2% respectively). The study in the Delaware soil having a 2.8% organic matter content (the Flanagan Illinois soil has 6.7% organic matter) also reported low material balance (32.8%) after 52 weeks. Based on the reported results, the Illinois soil having both a low sand content (12%) and a higher organic matter content (6.7%) had the highest material balance throughout the study. The Illinois Flanagan silt loam soil was also reported to allow DPX-F6025 to leach only moderately (in the soil leaching study) in comparison to Woodstown sandy loam and the Cecil sandy loam. Therefore, the material loss in the field dissipation study appears to correlate reasonably well with the leaching potential of DPX-F6025 and its degradates as observed in the soils column leaching studies. Unfortunately, the field dissipation study did not provide a good material balance and information to field depths of more than 32 cm although these depths are likely to contain leached DPX-F6025 and its degradates (the degradates were reported to have even a higher potential for leaching-most of the secondary degradates were not identified).

10.3 A. Study Identification: Anaerobic Aquatic Metabolism of $^{14}$C-Labeled DPX-F6025

The study was conducted by the Agricultural Chemicals Division of Du Pont, Research Division Experimental Station, Wilmington, Delaware by E. M. Venzon and P. T. Hardesty (Document No. AMR-322-85).

B. Materials and Methods:

Sterilized and unsterilized anaerobic pond water and sediments from two locations (Landenburg, PA and Bradenton, FL) were collected and stored in plastic bags. Portions of soils were dried and characterized (see attachment). Soil portions were autoclaved at 15 psi steam pressure to achieve sterilization. Individual samples were prepared by weighing 50 gm samples of hydrosoils in 250 ml plastic bottles. These samples were treated with a methylene chloride solution to give an application rate of 0.1 ppm of [$^{14}$C-phenyl]-DPX-F6025 or 0.1 ppm [$^{14}$C-pyrimidine]-DPX-F6025. After the solvent was evaporated, 100 ml of pond water were added to the sample, shaken, purged with nitrogen, capped and stored in a dark incubator at 25°C for 52 weeks. The pH of the pond water before mixing with the soil was 6.7 (6.5 for the Florida samples). The Florida sterile control samples were prepared by adding a pH 7 buffer solution of the radiolabeled DPX-F6025. Samples were taken at specified time intervals, centrifuged, and the water was decanted and analyzed by LSC. The soil was then extracted with 3x150 ml portions of $CH_3OH/(NH_4)_2CO_3$-2M, ("MA",3/1 v/v). The MA extraction solvent was then analyzed by LSC to determine the total radioactivity. Then it was concentrated under reduced pressure at 50°C to 1/4 of the original volume. The aqueous concentrate and an aliquot of the original aqueous phase were acidified to pH 1-2 with 85% phosphoric acid and was then quickly extracted with 3x150 portions of methylene chloride and both the aqueous and the $CH_2Cl_2$ were analyzed by LSC. A portion was co-chromatographed on TLC with DPX-F6025 and authentic samples of potential degradates. Bands of

radioactive material were detected and integrated. Levels of unextracted radiolabeled material were determined by combusting a 5 gm homogenized portion of the extracted soil, trapping and counting the evolved $^{14}CO_2$.

C. Reported Results:

In both soils (PA and FL), most of the radioactivity was found in the water fractions. The levels of bound radioactivity (measured by combustion) was larger in the Pennsylvania soil than in the Florida soil (in the FL soil most of the radioactivity was recovered in the aqueous and the methylene chloride extracts). The total recoveries in both soils ranged from 95% to 109% of the applied dose, averaging 99.8% for the PA samples and 104.7% for the FL samples. In the sterile control samples, most of the radioactivity was also found in the water and recoveries were consistently higher than 100%. Analysis of the methylene chloride extract of the acidified aqueous fractions indicated that the levels of intact DPX-F6025 decreased rapidly over the initial 7 weeks of the study and was found primarily in the aqueous phase. The half lives were estimated at 5-6 weeks for the Pennsylvania soil and 2-3 weeks for the Florida soil. On the other hand, degradation was much slower in both PA and FL sterile soils with half lives of 20 and 30 weeks (22 and 36 calculated values), respectively. The major metabolite in the non-sterile soils was demethylated DPX-F6025. On the other hand, DPX-F6025 degraded slower under sterile conditions to sulfonamide and saccharin via hydrolysis which was also the major degradation pathway observed in the aerobic soil degradation study. No demethylated products were detected at any sampling points for the sterile soils. In the PA soil after 52 weeks, 33% of the pyrimidine labeled dose was bound to the soil compared to 16% of the phenyl-labeled dose. Total recoveries for the PA soil samples averaged 94.5%. The identity of the degradates was confirmed by co-chromatography on TLC and by MS analysis.

D. Study Author's Conclusions:

The author concluded that the DPX-F6025 underwent anaerobic soil degradation by hydrolysis and microbial activity with half lives of 5-6 weeks in the PA soil and 2-3 weeks in the FL soil. The hydrolysis resulted in sulfonamide and pyrimidine amine and microbial degradation in demethylated DPX-F6025. The demethylated DPX-F6025 underwent hydrolysis at a much slower rate than the parent compound. Under sterile conditions the primary degradative pathway for DPX-F6025 was chemical hydrolysis and the half lives of DPX-F6025 were 26-40 weeks at the studied soils. Recoveries of over 100% were attributed to probable errors in applying the radiolabeled material.

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

The study was able to trace 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 2-6 weeks depending on the soil. The anaerobic degradation in the non-sterile PA soil resulted after 26 weeks in 58.9% of demethylated DPX-F6025 and only 0.8% of the parent compound, for a total of 83.7%. On the other hand, the aerobic metabolism study reviewed ~~earlier~~ concluded that chemica

in the other 9/9/85 evaluation

hydrolysis was the major degradative pathway. The aerobic soil metabolism study also concluded that microbial degradation was not an important degradative pathway for DPX-F6025 under these conditions. On the other hand, demethylated DPX-F6025 was reported present between 44.7-45.5% at weeks 34-41 of the crop rotation study, indicating a high microbial activity. The data show demethylated DPX-F6025 to form and to be the major product under anaerobic conditions but not under aerobic soil conditions.

10.4 A. Study Identification: Aqueous Photolysis of $^{14}C$ DPX-F6025.

The study was done at the Agricultural Chemical Department, Research Division Experimental Station of du Pont at Wilmington, Delaware by Priscilla L. Friedman (Document No. AMR-299-84).

B. Materials and Methods:

A stock solution of 100 ppm DPX-F6025 was prepared by dissolving 2.5 mg of the [phenyl-$^{14}C$ (U)]-DPX-F6025 or [(2-pyrimidine)-$^{14}C$]-DPX-F6025 in 25 ml of acetonitrile/sterilized water (40/60, v/v). Test solutions of 5 ppm and 0.5 ppm were prepared by diluting aliquots (15 ml or 1.5 ml) of the stock solution to 300 ml with sterilized buffer solutions. Buffer solutions of pH 5, 7 and 9 were sterilized in an autoclave for 1 hr at 15 psi steam pressure on three consecutive days. All glassware were sterilized by the same procedure. The test solutions were placed in separate 400 ml beakers and covered with flat quartz lids to retard evaporation while permitting transmission of UV light. The solutions were stirred continuously by magnetic stirrers and kept at 25°C by a thermostated bath. A bank of 6 fluorescent sunlamps alternating with 6 fluorescent black lamp was set 6 inches above the surface of the test solutions. The avarage light intensity (300-450 nm) measured by a spectro radiometer was 45.5 watts/$m^2$ at a distance of 4.5 inches (see attachment). That was about half of the energy emitted from natural sunlight as measure by the same instrument (see attached energy spectra). A dark control solution of the $^{14}C$-phenyl labeled DPX-F6025 was prepared by dissolving 3 mg of the radiolabeled compound in 5 ml of acetone and adding 25 ml of sterilized water. Aliquots were then added to 100 ml of sterilized buffer solutions to prepare 5 and 0.5 ppm solutions of the test compound. A 520 ppm control solution of the $^{14}C$-pyrimidine labeled analogue was prepared by dissolving 10.4 mg of the labeled DPX-F6025 in 5 ml of acetone and diluting it as needed. Aliquots were taken at specified time intervals and their pH was adjusted to 4 with acetic acid prior to analysis. Then, the solutions were extracted three times with methylene chloride. The combined methylene chloride extracts were dried over anhydrous magnesium sulfate, filtered and concentrated under a flow of nitrogen in a 45°C water bath. The concentrated methylene chloride extracts were analyzed by TLC and/or HPLC, as well as, by HPLC-MS via thermospray mass spectrometry.

C. Reported Results:

The parent compound degraded in both exposed and non-exposed solutions. However, DPX-F6025 degraded much faster under exposed conditions with a half life of two days in the various concentrations and pH range of 5-9. The dark samples degraded with half lives of 18-30 days depending

on the pH. The degradation products were diametrically different in the photolyzed and dark solutions. Photolysis resulted in rearrangement and the proposed rearrangement products were identified by mass spectrometry and shown in the attached scheme. The experiment provided a complete account for the total $^{14}C$ radiolabeled material that was present in the DPX-F6025 solutions throughout the study.

D. Study Author's Conclusions:

The study author concluded that the photodegradation of DPX-F6025 in sterilized buffers at pH 5, 7 and 9, at 25°C proceeded fast with a half life of 2 days. The degradation products were identified as rearrangement products of DPX-F6025 and were completely different from the product obtained via hydrolytic degradation of the dark control samples. The dark control samples degraded much slower with half lives of 18-30 days depending on the pH. Since the overall recovery of $^{14}C$ averaged 101%, no volatile radiolabeled degradation products were produced from any of the test solutions.

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

In the reviewer's opinion the study should have been conducted under natural sunlight conditions. The light used in the study had most of its intensity in the UV range and was not shown to be comparable to that of natural sun light. The identification of rearrangement products were based completely on HPLC-MS. The study clearly confirmed by co-chromatography on HPLC that the photodegradation product was not the dechloro DPX-F6025 and/or any of the hydrolysis products. Although the reviewer did not find reasons to disagree with the conclusions drawn from the mass spectral data of the rearrangment product, additional conformatio by co-chromatography and/or $^{13}C$ NMR is needed. In addition, hydrolysis degradation studies of the rearrangement product might be helpful in confirming the identity of the rearrangement product and its fate in the environment. A major concern was raised over the use of co-solvents although the solubility of DPX-F6025 in water was reported as 1200 ppm at 20°C at pH 7. The use of a co-solvent potentially varied the experimental conditions from those normally obtained in the environment. Since a co-solvent was used, it was not clear why acetone was the co-solvent of choice in the dark control sample and acetonitrile in the photolysis sample. Additionally, the concentration of acetonitrile in solution varied in the 5 ppm solution from that in the 0.5 ppm solution due to improper dilution (the sample should have been diluted with identical solvent to that of the stock solution in order to have identical solvent conditions). It is in the reviewer's opinion that a new study should be conducted for registration and a co-solvent used only when necessary and when demonstrated that it did not affect the experimental results (particularly by serving as a potential photosensitizer).

11. COMPLETION OF ONE LINER:

Not completed.

12. CBI APENDIX:

None