#5735

Shaughnessy No.: _____

Due date: 01 NOV 1984

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

From: Samuel M. Creeger, Chief
Environmental Chemistry Review Section 1
Exposure Assessment Branch
Hazard Evaluation Division TS-769c

Attached, please find the EAB review of:

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

Chemical: DPX-M6316

Type Product: Herbicide

Product Name: DPX-M6316

Company Name: Du Pont

Submission Purpose: EUP on wheat and barley

ZBB Code: Other

Action Code: 710

Date In: 8/30/84

EAB No.: 4552

Date Completed: 11/1/84

TAIS (Level II)	Days
61	10

Deferrals To:

_____ Ecological Effects Branch

_____ Residue Chemistry Branch

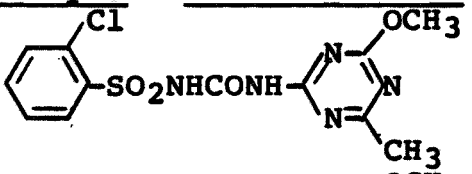
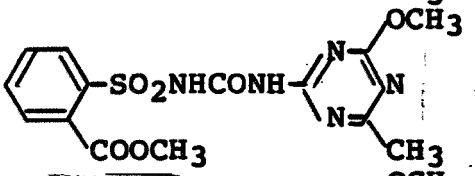
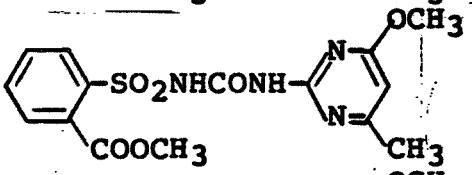
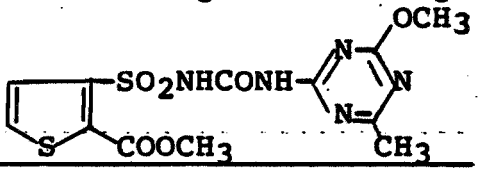
_____ Toxicology Branch

1.0 INTRODUCTION

Du Pont has requested an EUP (Reg. No.352-EUP-RER) to use its new herbicide, DPX-M6316, on wheat and barley.

The registrant proposes that a total of 840 pounds of the product (630 pounds ai) will be tested in 34 states across the US (12,600 acres) with an average trial size of about 20 acres per location during a three-year period (1985-1987). The proposed test program is appended.

Similar chemicals has already been filed in the Agency by the registrant and these are summarized in the following table.

Dupont Code #	Common Name	Trade Name	EAB Shaughnessy #	Structural Formular
DPX-4189	Chlorsulfuron	GLEAN	118601	
DPX-6376	Metsulfuron methyl	ALLY	122010	
DPX-5648	Sulfometuron methyl	OUST	122001	
DPX-6316	Not yet estab.			

1.1 Chemical

Chemical name: Methyl 3[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]-2-thiophenecarboxylate.

Structral formula: See section 1.0, above.

Empirical formula: $C_{12}H_{13}N_5O_6S_2$ (MW 387.40)

Common name: Not yet established.

Trade name: Not yet established.

1.2 Physical and Chemical Properties (Active Ingredient)

Color: white

Physical state: crystaline solid

Ordor: none

Melting Point: 186°C

Density: 1.49 g/cc

Solubility (25°C):

Water (pH 4.0)	24	mg/L
" (pH 5.0)	260	mg/L
" (pH 6.0)	2400	mg/L
Acetone	11.9	mg/L
Acetonitrile	7.3	mg/L
Ethanol	0.9	mg/L
Ethyl Acetate	2.6	mg/L
Hexane	<0.1	mg/L
Methanol	2.6	mg/L
Methylene chloride	27.5	mg/L
Xylenes	0.2	mg/L

Vapor pressure: 2.7×10^{-6} mm Hg at 25°C

Dissociation constant: 4.0 (pKa of the acid)

Octanol/Water partition coefficient: 0.027

pH: 4.0 (slurry in water)

Stability: Stable to metals and light. Decomposes on melting. In solution, is very stable in methylene methylene chloride and ethyl acetate, moderately stable in methanol, and relatively unstable in acetone and acetonitrile. The half-life in an aqueous photolysis is estimated to be 1 to 5 days.

1.3 Physical and Chemical Properties (End-use Product)

Color: tan

Physical state: granular solid (<0.03 % below 37 μ)

Odor: none

Density: 0.593 g/ml

pH: 5.5 (2 % w/w in distilled water)

Oxidizing/reducing action: none

Flammability: not flamable

Explodability (premix):
Minimum ignition energy 0.11 joules
Lower explosive limit 0.25 g/l
Maximum explosion pressure 102 psi
Maximum rate of pressure rise 1469 psi/sec
Minimum oxygen content 14.5 %

Stroage stability:

Initial	76.0 ± 0.8 % DPX-M6316
24 Days at -6°C	75.1 ± 0.8 % DPX-M6316
24 Days at 45°C	74.8 ± 0.8 % DPX-M6316

Corrosion characteristics: Compatible with polyethylene and polypropylene.

2.0 DIRECTIONS FOR USE

A copy of the proposed experimental labeling is appended. In short, 1/6 to 1-1/3 oz of DPX-M6316 (75 % ai) per acre is applied to wheat (including durum) or barley after the crop is in the 2-leaf stage but before "boot" stage. DPX-M6316 (1/6 to 1-1/3 oz per A) plus Du pont Ally® Herbicide (1/20 to 1/15 oz per A) may be applied as a tank mixture.

3.0 DISCUSSION OF DATA

Some of the environmental fate data included in this submission (Acc. No. 072846) were obtained from chlorsulfuron (DPX-W4189) or metsulfuron methyl (DPX-T6376). These chemicals have the same triazine moiety in thier structure as in DPX-M6316.

3.1 Hydrolysis

3.1.1 Hydrolysis of DPX-M6316[thiophene-2-^{14}C]. M. K. Koeppe and B. C. Rhodes, Undated, Du Pont Document No. AMR-224-84.

Experimental

DPX-M6316[thiophene-2-^{14}C] (23.1 µCi/mg, >99 % purity) was subjected to hydrolysis at 0.5 and 5.0 ppm, pH's 5, 7 and 9 (phthalate, phosphate and borate buffers, respectively) and 25°C under sterile conditions in darkness.

Aliquots of each solution (20 ml) were removed at 0 time and days 1, 2, 3, 6, 8, 10, 14, 21 and 30. Additional samples were taken from the two pH 5 solutions at 1 and 4 hours. The pH of each solution was monitored at days 0, 8, 14, 21 and 30.

Four 250-µl aliqouts were taken from each solution to determine the total radioactivity by LSC. After acidification to pH 3-4 with acetic acid, the remainder of each sample was extracted with methylene chloride (3x). Aliquots of the combined organic fraction and the aqueous phase were radioassayed. The organic phase was concentrated and analyzed by TLC (silica gel 60 F254, 0.25 mm thickness, solvent system CH_2Cl_2/MeOH/NH_4OH 29/10/1) and autoradiography. Aliquots (200 ul) of the methylene chloride concentrates were evaporated to dryness and redissolved in acetonitrile. These acetonitrile solutions were analyzed by HPLC. Radioactive fractions corresponding to the retention times of standard DPX-M6316, methyl 3-(aminosulfonyl)-2-thiophene carboxylate and two unidentified compounds were extracted with CH_2Cl_2 and the extracts analyzed by MS.

Results

Hydrolysis of DPX-M6316 at pH 5, 7 and 9 produced the same primary product, methyl 3-(aminosulfonyl)-2-thiophene carboxylate, but with different rates. More than 60 % of the applied radioactivity was found in the product after 4 days in pH 5 buffer, about 9 % in pH 7 buffer and 5-8 % in pH 9 buffer. The half-life was estimated to be 4-6 days in pH 5 buffer solutions. At pH's 7 and 9, hydrolysis was significantly slower; more than 80 % of the applied activity remained as parent compound after 30 days of hydrolysis. No half-life estimations were reported at these pH's.

Tables 1-3 show the % activity found in the parent and the hydrolysis products. Two additional hydrolysis products were detected in pH 5 solutions; The major unknown, H 1 (35 % of the total radioactivity in 5.0 ppm solution by 21 days) and the other unknown, H 2 (8.2 % at day 6), could not be identified. Possibility to be one of the following compounds (structures, see figure 1 in section 3.2.1) were excluded by co-chromatography:

- o 3-[[[[(4-hydroxy-6-methyl-1,3,5-thiazin-2-yl)amino]-carbonyl]amino]sulfonyl]-2-thiophenecarboxylic acid,
- o methyl 3-[[[[(4-hydroxy-6-methyl-1,3,5-thiazin-2-yl)-amino]carbonyl]amino]sulfonyl]-2-thiophenecarboxylate,
- o 3-(aminosulfonyl)-2-thiophenecarboxylic acid,
- o thieno[2,3-d]isothiazol-3(2H)-one 1,1-dioxide

Recoveries were excellent except in pH 5, 0.5 ppm solution incubated longer than 8 days. About 80 % recovery was reported in samples taken later than day 8. It is actually about 70 % of the 0 time recovery.

Figure 1 presents the proposed hydrolytic pathway of DPX-M6316 in acidic conditions.

TABLE 1

HYDROLYSIS OF DPX-M6316 AT pH 5

Sampling Day	% Originally Applied Radioactivity Remaining As: DPX-M6316	Methyl 3-(aminosulfonyl)-2-thiophenecarboxylate	H1	H2	Polars[a]	Total Recovery
Initial Concentration 0.5 ppm						
0	112.5	0.9	<0.1	<0.1	0.7	114.1
0.04	109.8	0.3	<0.1	<0.1	0.8	110.9
0.17	102.9	2.0	<0.1	<0.1	1.7	106.6
1	93.0	7.0	0.8	<0.1	2.7	103.5
2	81.3	10.2	0.6	3.6	3.5	99.2
3	68.3	20.7	<0.1	1.3	4.5	94.8
6	50.1	35.5	5.6	2.3	5.4	98.9
8	36.9	37.3	2.1	0.8	5.6	82.7
10	27.8	45.4	<0.1	1.9	5.1	80.2
14	13.6	60.5	<0.1	3.8	4.5	82.4
21	6.0	64.7	5.0	<0.1	3.9	79.6
30	3.0	62.4	8.4	4.4	4.1	82.3
Initial Concentration 5.0 ppm						
0	106.1	0.3	<0.1	<0.1	1.5	107.9
0.04	105.7	1.2	<0.1	1.4	1.5	109.8
0.17	100.2	2.9	<0.1	1.5	3.1	107.7
1	82.1	11.7	2.9	2.0	4.3	103.0
2	75.0	18.4	7.3	1.8	5.9	108.4
3	62.6	23.0	8.7	6.9	6.5	107.7
6	36.0	39.0	17.5	8.2	6.4	107.1
8	24.9	48.6	9.2	3.4	6.3	92.4
10	18.2	57.3	24.0	3.4	6.2	103.1
14	8.5	56.8	27.5	4.3	5.2	102.3
21	2.8	62.6	34.8	1.1	5.0	106.3
30	4.0	64.1	32.0	<0.1	5.1	105.2

[a] Percent of applied radioactivity remaining in the acidified aqueous phase after the methylene chloride extractions.

Section 3.1.1

TABLE 2

HYDROLYSIS OF DPX-M6316 AT pH 7

Sampling Day	% Originally Applied Radioactivity Remaining As: DPX-M6316	Methyl 3-(aminosulfonyl)-2-thiophenecarboxylate	Polars[a]	Total Recovery %
Initial Concentration 0.5 ppm				
0	103.1	0.7	1.2	105.0
1	101.2	0.9	0.2	102.3
2	102.4	1.1	0.2	103.7
3	99.7	2.2	0.3	102.2
6	101.1	3.3	0.4	104.8
8	99.0	3.5	0.7	103.2
10	100.7	4.0	0.8	105.5
14	97.3	8.3	1.0	106.6
21	94.1	11.0	1.6	106.7
30	92.0	9.7	2.4	104.1
Initial Concentration 5.0 ppm				
0	103.6	<0.1	0.1	103.7
1	98.9	0.9	0.3	100.1
2	99.9	1.2	0.3	101.4
3	101.0	1.7	0.4	103.1
6	102.4	2.8	0.6	105.8
8	100.1	3.7	0.9	104.7
10	99.6	4.5	1.0	105.1
14	97.0	5.7	1.4	104.1
21	95.3	6.5	2.2	104.0
30	89.5	9.4	2.9	101.8

[a] Percent of applied radioactivity remaining in the acidified aqueous phase after th methylene chloride extractions.

Section 3.1.1
TABLE 3

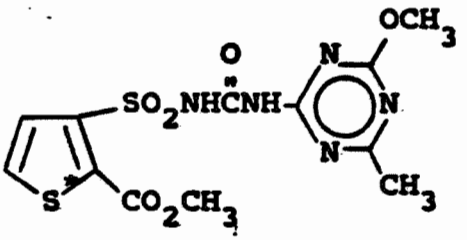
HYDROLYSIS OF DPX-M6316 AT pH 9

Sampling Day	% Originally Applied Radioactivity Remaining As: DPX-M6316	Methyl 3-(aminosulfonyl)-2-thiophenecarboxylate	Polars[a]	Total Recovery (%
Initial Concentration 0.5 ppm				
0	104.5	<0.1	0.3	104.8
1	89.4	<0.1	0.7	90.1
2	91.5	<0.1	1.1	92.6
3	92.0	1.1	1.3	94.4
6	90.0	2.5	1.4	94.8
8	91.1	2.7	1.7	95.5
10	91.8	2.3	1.9	96.0
14	90.0	5.3	2.2	97.5
21	85.5	7.6	3.6	96.7
30	82.3	8.2	4.8	95.3
Initial Concentration 5.0 ppm				
0	110.6	1.0	0.4	112.0
1	108.8	0.3	1.6	110.7
2	107.5	0.1	2.1	109.7
3	104.8	0.8	3.2	108.8
6	101.6	1.1	4.5	107.2
8	97.5	1.5	5.6	104.6
10	94.8	1.7	5.9	102.4
14	94.6	2.7	6.7	104.0
21	92.7	3.8	7.7	104.2
30	87.6	4.9	9.7	102.2

[a] Percent of applied radioactivity remaining in the acidified aqueous phase after the methylene chloride extractions.

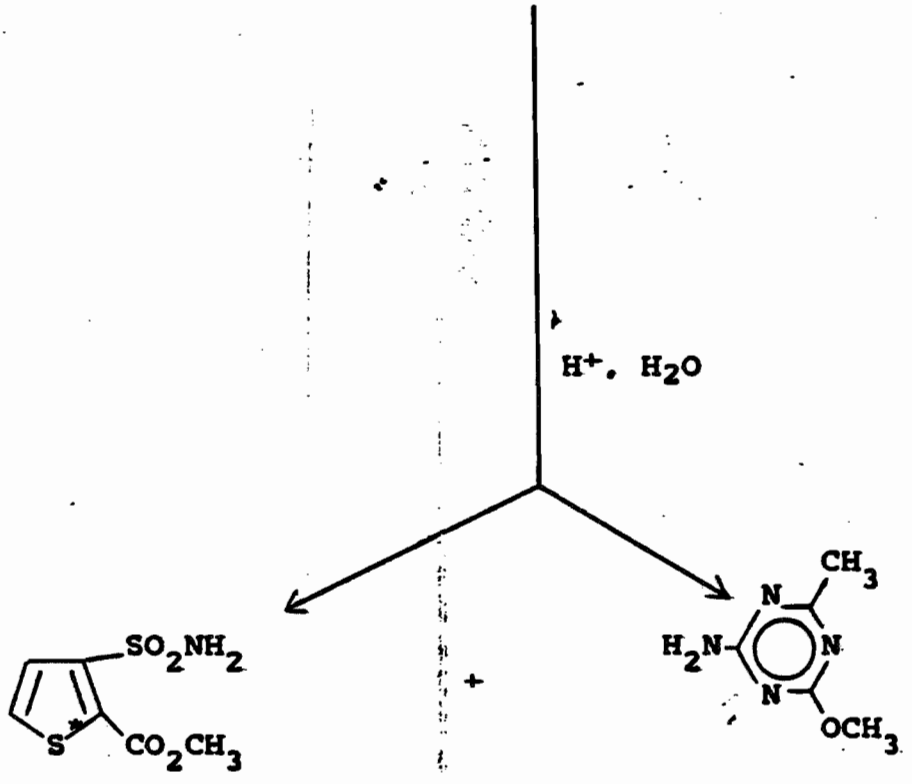
Section 3.1.1
FIGURE 1

HYDROLYSIS OF DPX-M6316



DPX-M6316

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



Methyl 3-(aminosulfonyl)-2-thiophenecarboxylate

2-amino-4-methoxy-6-methyl-1,3,5-triazine

* Position of the ^{14}C label

Conclusion

DPX-M6316 appears to undergo hydrolysis under acidic conditions (pH 5) to give methyl 3-(aminosulfonyl)-2-thiophenecarboxylate as a major product with a half-life about 4-6 days. Hydrolysis under neutral to basic conditions (pH's 7 and 9) takes place significantly slower.

However, this study cannot be accepted as is because the other degradation products, especially H 1 which comprised up to 35 % of the applied radioactivity in the pH 5 solution, were not identified. Also, the fate of the triazine moiety of the compound need to be traced.

3.1.2 Hydrolysis of ^{14}C-Labeled DPX-W4189. J. C-Y. Han, Undated, Du Pont Document No. AMR-39-81.

This study has an EPA accession No.245878 from the previous submission in connection with chlorsulfuron registration, but EAB file on chlorsulfuron does not have the record of the review of the study. Instead, a hydrolysis study on chlorsulfuron with Du Pont Document No. AMR-08-80A was reviewed (11/17/80) and the registrant was recommended to submit a revised report.

Experimental

DPX-W4189 (^{14}C-phenyl and ^{14}C-triazine) was subjected to hydrolysis at pH's 4, 7 and 9, at 10 and 20°C and at 1.0 and 10.0 ppm in the dark. Sterile conditions were not mentioned.

Small aliquots of each solution were taken for LSC/TLC analyses at one week intervals for 4 weeks. Standards of postulated hydrolysis products were chromatographed on the same plates, scanned for radioactivity and visualized under UV. The areas of silica gel corresponding to standards were removed, extracted (methanol) and confirmed by MS. Two more polar compounds from 4 week's hydrolysis (triazine-labeled) were reacted with diazomethane and analysed by MS.

Results

In all samples the total loss of radioactivity was <5 %. AT pH's 7 and 9, DPX-W4189 was found to be stable (<5 % decomposition). However at pH 4, DPX-W4189[^{14}C-triazine] degraded to 2-amino-4-methoxy-6-methyl-1,3,5-triazine which further degraded to 2-amino-4-hydroxy-6-methyl-1,3,5-triazine and 2,4-dihydroxy-6-methyl-1,3,5-triazine as confirmed by MS after methyl derivatization with diazomethane.

The decline of DPX-W4189 at pH 4 is shown in table 1. The half-life was estimated to be one week at 20°C and about 10-14 days at 10°C.

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Section 3.1.2

TABLE I

HYDROLYSIS OF ^{14}C-DPX-W4189 AT pH 4

(% of Intact ^{14}C-DPX-W4189 Recovered)

Sample			Exposure Time				
conc. (ppm)	^{14}C-label position	Temperature (°C)	0 Week	1 Week	2 Week	3 Week	4 Week
1	phenyl	10	100	78	41	34	30
10	phenyl	10	100	59	28	19	13
1	phenyl	20	100	40	21	7	2
10	phenyl	20	100	65	22	6	2
1	triazine	10	100	79	28	20	16
10	triazine	10	100	63	26	17	15

Section 3.1.2

Figure 1

Hydrolysis of ^{14}C-Labeled DPX-W4189 in Acidic Solutions

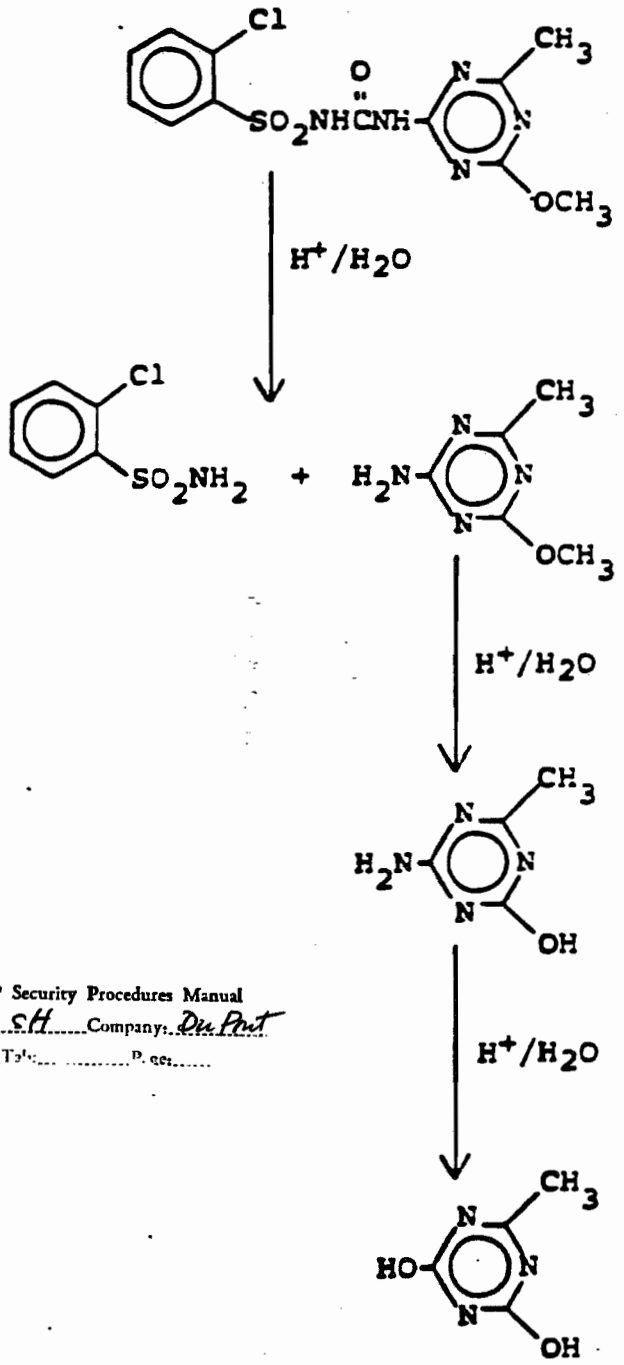


Figure 1 showes the hydrolysis of ^{14}C-labeled DPX-W4189 in acidic solutions.

Conclusion

DPX-4189 is stable to hydrolysis at pH's 7 and 9 showing <5 % degradation in 4 weeks. At pH 4 the chemical degrades to 2-amino-4-methoxy-6-methyl-1,3,5-triazine and 2-chloro-chlorobenzenesulfonamide showing a half-life of one week at 20°C. The triazine moiety undergoes futher hydrolysis with a very low rate to give 4-hydroxy and 2,4-dihydroxy compounds.

Although this study did not follow the Guidelines, it shows the fate of the triazine moiety of the compounds in this class.

3.1.3 Hydrolysis of ^{14}C-4-Methoxy-6-Methyl-1,3,5-triazine-2-Amine. P. L. Friedman, Undated, Du Pont Document No. AMR-136-83.

This study was previously reviewed (see section 3.1 of EAB review dated 7/12/84 under DPX-T6376, ALLY®, Shaughnessy No. 122010) and was considered to be adequate to describe the fate of triazine moiety.

3.2 Aerobic Soil Metabolism

3.2.1 Aerobic Soil Metabolism of DPX-M6316[Thiophene-2-^{14}C]. C. Rapisarda, Undated, Du Pont Document No. AMR-236-84.

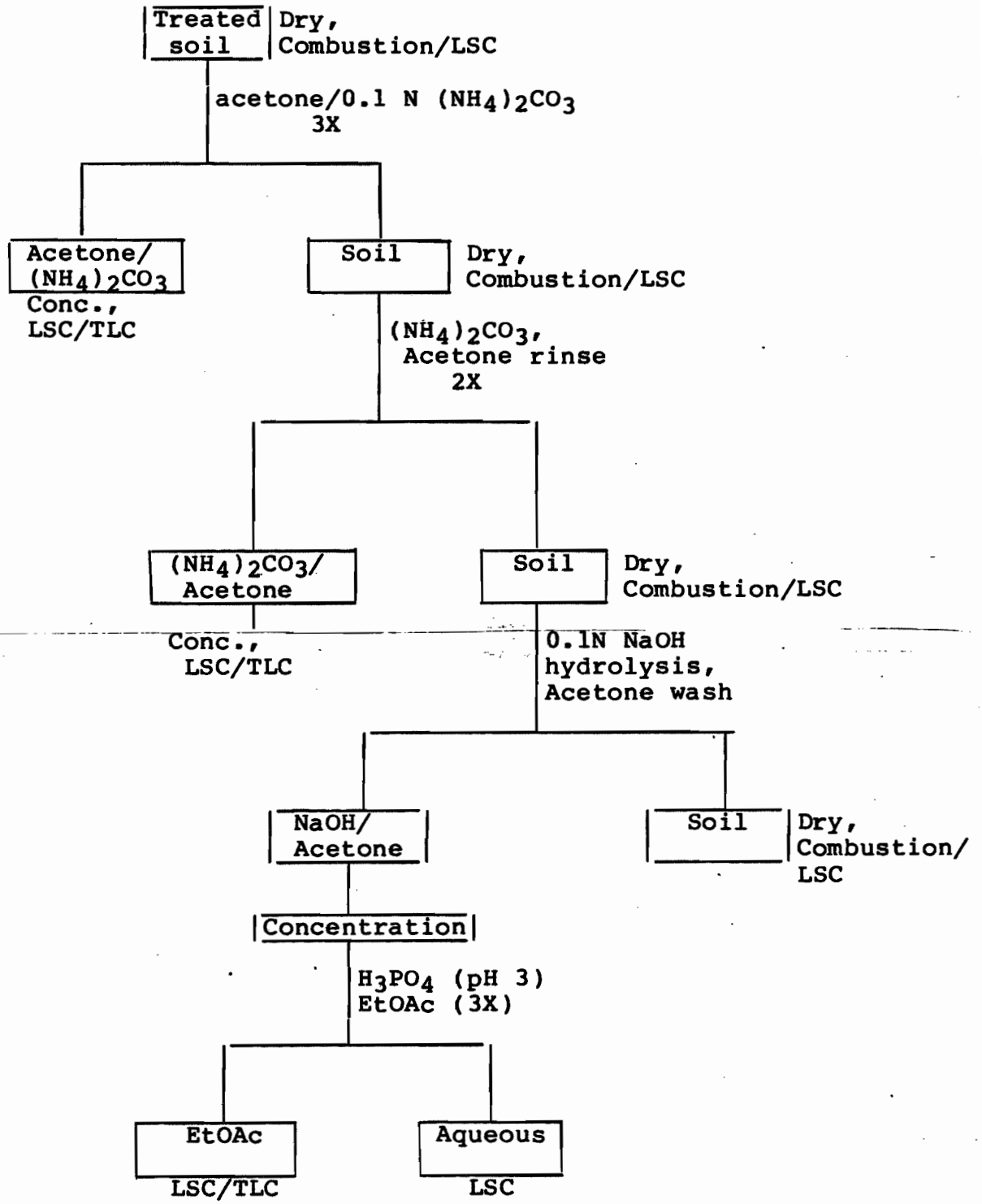
Duplicate of non-sterile and sterilized soil samples (soil charateristics are described on p.14), equivalent to 50 g oven-dry weight, were weighed into the 250-ml E-meyer flask side of biometers and 10 ml of 0.1 N NaOH were added to the side arms. All soils were treated with 2.53 ug (0.058 uCi) of ^{14}C-DPX-M6316 (80 g ai/ha) and moistened to 70 % of field maximum moisture capacity. After the samples were thoroughly mixed and oxygen was introduced, the flasks were closed and incubated at 25°C in the dark. Duplicate non-sterile controls without ^{14}C-DPX-M6316 were also done under the same conditions. The soil metabolism of ^{14}C-glucose at 2 ppm was checked under the same experimental conditions. All flasks were opened weekly to add oxygen to the system (see recommendation for discussion on the opening of the flask).

The caustic solutions were radioassayed by LSC. After the trapped CO_2 was precipitated with $BaCO_3$, the supernatants were also assayed for unprecipitated radioactivity.

The test soil samples were taken after 0, 0.5, 1, 2, 3, 4, 6, 8, 11, 14 and 20 weeks of aging and the sterile control samples were taken after 2, 4, 6, 8 and 20 weeks.

Each soil sample was extracted and analyzed according to the scheme in the following page.

B


Treated soil
Dry, Combustion/LSC
acetone/0.1 N $(NH_4)_2CO_3$ 3X
Acetone/ $(NH_4)_2CO_3$
Conc., LSC/TLC
Soil
Dry, Combustion/LSC
$(NH_4)_2CO_3$, Acetone rinse 2X
$(NH_4)_2CO_3$/ Acetone
Conc., LSC/TLC
Soil
Dry, Combustion/LSC
0.1N NaOH hydrolysis, Acetone wash
NaOH/ Acetone
Soil
Dry, Combustion/ LSC
Concentration
H_3PO_4 (pH 3) EtOAc (3X)
EtOAc
LSC/TLC
Aqueous
LSC

To identify metabolites, non-sterile Gardena silt loam soil (60 g) was treated with ^{14}C-DPX-M6316 at 10 ug/g and incubated at 30°C for 7 days. The soil was extracted with methanol/2M $(NH_4)_2CO_3$ (3/1), and the solvent evaporated to dryness. The residue was resuspended in water, acidified with d-HCl to pH 3 and extracted with CH_2Cl_2. The methylene chloride extract was radioassayed and evaporated to dryness. The residue, dissolved in water, was analyzed by HPLC and then MS.

Results

The soil characteristics are shown in the following table.

Component	Keyport Silt Loam (Newark, DE)	Flanagan Silt Loam (Rochelle, IL)	Gardena Silt Loam (Rodger, ND)
Sand (2000-50 um) %	12	2	43
Silt (50-2 um) %	83	81	51
Clay (<2 um) %	5	17	6
Organic matter %	7.5	4.3	5.0
Nitrogen %	0.30	0.26	ND
pH	5.2	5.4	8.1
Cation Exchange capacity (meq/100 g)	15.5	21.2	ND

Overall distribution of radioactivity is summarized in tables 1 - 4.

In the non-sterile studies, the percent extractables decreased rapidly with subsequent increase in the percent $^{14}CO^2$ and unextractables.

In the sterilized soil studies, no CO_2 was evolved and extractables decreased slowly with a corresponding increase in unextractables.

After 20 weeks of aging, 44 % of the applied ^{14}C was recovered as CO_2 from the Keyport soil and 31 % from the Flanagan soil.

The estimated half-lives were less than 2 days in Keyport soil (24 days in sterile soil) and 6 days in Flanagan soil (32 days in sterile soil).

Five metabolites were identified and the proposed metabolic pathway of DPX-M6316[thiophene-2-^{14}C] is shown in figure 1.

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Section 3.2.1

TABLE 1

DISTRIBUTION OF RADIOACTIVITY IN KEYPORT SILT LOAM TREATED WITH DPX-M6316 [THIOPHENE-2-^{14}C][a]

Incubation Time (weeks)	% of Recovered Radioactivity[b]					
	Non-sterile			Sterilized		
	$^{14}CO_2$	Extracted[c]	Unextracted[d]	$^{14}CO_2$	Extracted[c]	Unextracted[d]
0	--	99.9	0.1			
0.5	11.7	80.0	8.3			
1	23.4	65.4	11.2			
2	28.7	46.3	25.0	0.0	99.1	0.9
3	30.8	50.3	18.9			
4	31.9	41.7	26.4	0.0	99.1	0.9
6	34.7	23.1	42.2	0.0	97.8	2.2
8	35.3	29.1	35.6	0.0	97.7	2.3
11	38.8	15.2	46.0			
14	39.6	23.4	37.0			
20	43.6	18.3	38.1	0.0	93.9	6.1

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a Keyport soil was treated with 51 ppb of DPX-M6316 [thiophene-2-^{14}C] and maintained at 70% of its moisture holding capacity during the incubation at 25 °C in the dark.

b On an average, ≥99% of the calculated applied radioactivity was recovered.

c Extracted portion, sum of the extracts.

d Unextracted portion, consisting of bound material, possibly incorporated ^{14}C, and caustic hydrolyzable ^{14}C of high polarity.

Section 3.2.1

TABLE 2

DISTRIBUTION OF RADIOACTIVITY IN FLANAGAN SILT LOAM TREATED WITH OPX-M6316 [THIOPHENE-2-^{14}C][a]

Incubation Time (weeks)	% of Recovered Radioactivity[a]					
	Non-sterile			Sterilized		
	$^{14}CO_2$	Extracted[c]	Unextracted[d]	$^{14}CO_2$	Extracted[c]	Unextracted[d]
0	-	99.8	0.2			
0.5	0.7	98.0	1.3			
1	2.5	94.4	3.1			
2	5.5	92.6	1.9	0.0	99.6	0.4
3	8.1	89.2	2.7			
4	10.9	85.7	3.4	0.0	99.2	0.8
6	13.9	66.2	19.9	0.0	96.4	3.6
8	16.9	66.7	16.4	0.0	95.3	4.7
11	21.7	54.9	23.4			
14	26.7	43.5	29.8			
20	31.0	46.5	22.5	0.0	87.2	12.8

a Flanagan soil was treated with 51 ppb of OPX-M6316 [thiophene-2-^{14}C] and maintained at 70% of its moisture holding capacity during the incubation at 25°C in the dark.

b On an average, ≥99% of the calculated applied radioactivity was recovered.

c Extracted portion, sum of the extracts.

d Unextracted portion, consisting of bound material, possibly incorporated ^{14}C, and caustic hydrolyzable ^{14}C of high polarity.

Section 3.2.1

TABLE 3

COMPOSITION OF RADIOACTIVITY IN KEYPORT SOIL EXTRACTS[a]

^{14}C-Compounds[b]	Percent of the Recovered Radioactivity[c], at Weeks										
	0	0.5	1	2	3	4	6	8	11	14	20
Non-sterile Soils											
DPX-M6316	97.1	15.5	7.5	7.9	3.1	2.4	1.6	2.5	1.4	2.2	1.6
Metabolites A+B	0.3	15.1	17.7	16.1	20.1	10.6	6.1	8.5	4.8	7.1	6.6
Metabolite C	1.2	3.3	2.3	1.9	2.1	5.8	2.6	4.0	1.6	1.7	0.5
Metabolite D	0.8	18.5	8.0	2.8	2.0	3.6	3.9	4.2	1.2	3.2	2.8
Metabolite E	0.3	24.5	29.6	16.6	20.5	17.4	7.0	8.3	2.6	6.6	4.1
Polar Material	0.2	3.1,	0.3	1.0	2.5	1.9	3.4	1.6	3.6	2.6	2.7
Total extracted	99.9	80.0	65.4	46.3	50.3	41.7	23.1	29.1	15.2	23.4	18.3
Sterile Soils											
DPX-M6316				66.0		41.4	35.3	25.5			7.7
Metabolites A+B				2.4		2.1	2.2	2.5			6.5
Metabolite C				18.7		31.1	35.5	43.1			41.8
Metabolite D				5.0		14.5	15.5	15.7			25.0
Metabolite E				4.1		7.9	8.5	10.5			12.1
Polar Material				2.9		2.1	0.8	0.4			0.8
Total extracted				99.1		99.1	97.8	97.7			93.9

a The Keyport silt loam soils were treated with 51 ppb of DPX-M6316 [thiophene-2-^{14}C] and maintained at 70% of its moisture holding capacity during the incubation at 25°C in the dark.

b Structures and Chemical Abstracts names of these compounds are shown in Figure 1.

c On the average, ≥99% of the calculated applied radioactivity was recovered.

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Section 3.2.1

TABLE 4

COMPOSITION OF RADIOACTIVITY IN FLANAGAN SOIL EXTRACTS[a]

^{14}C-Compounds[b]	Percent of the Recovered Radioactivity[c], at Weeks										
	0	0.5	1	2	3	4	6	8	11	14	20
Non-sterile Soils											
DPX-M6316	93.5	74.0	53.8	15.1	13.5	11.2	8.1	7.6	3.2	2.5	2.6
Metabolites A+B	1.3	5.5	11.5	23.7	27.8	22.9	16.2	18.2	15.3	14.3	18.1
Metabolite C	1.4	4.7	4.2	10.5	5.7	5.3	2.9	2.3	1.9	2.3	0.8
Metabolite D	2.1	3.5	7.2	12.8	11.5	13.5	10.5	15.5	6.0	3.8	5.8
Metabolite E	1.3	8.8	15.0	26.7	26.1	28.6	24.7	21.1	22.9	13.3	11.4
Polar Material	0.2	1.5	2.7	3.8	4.6	4.2	3.8	1.9	5.6	7.3	7.8
Total Extracted	99.8	98.0	94.4	92.6	89.2	85.7	66.2	66.7	54.9	43.5	46.5
Sterile Soils											
DPX-M6316				72.8		51.1	40.9	47.7			11.6
Metabolites A+B				3.2		3.6	4.5	8.1			12.9
Metabolite C				10.6		21.1	25.5	12.7			22.6
Metabolite D				8.8		15.2	15.1	15.3			21.1
Metabolite E				3.7		6.5	6.8	11.0			14.1
Polar Material				0.5		1.6	3.6	0.5			4.8
Total Extracted				99.6		99.2	96.4	95.3			87.2

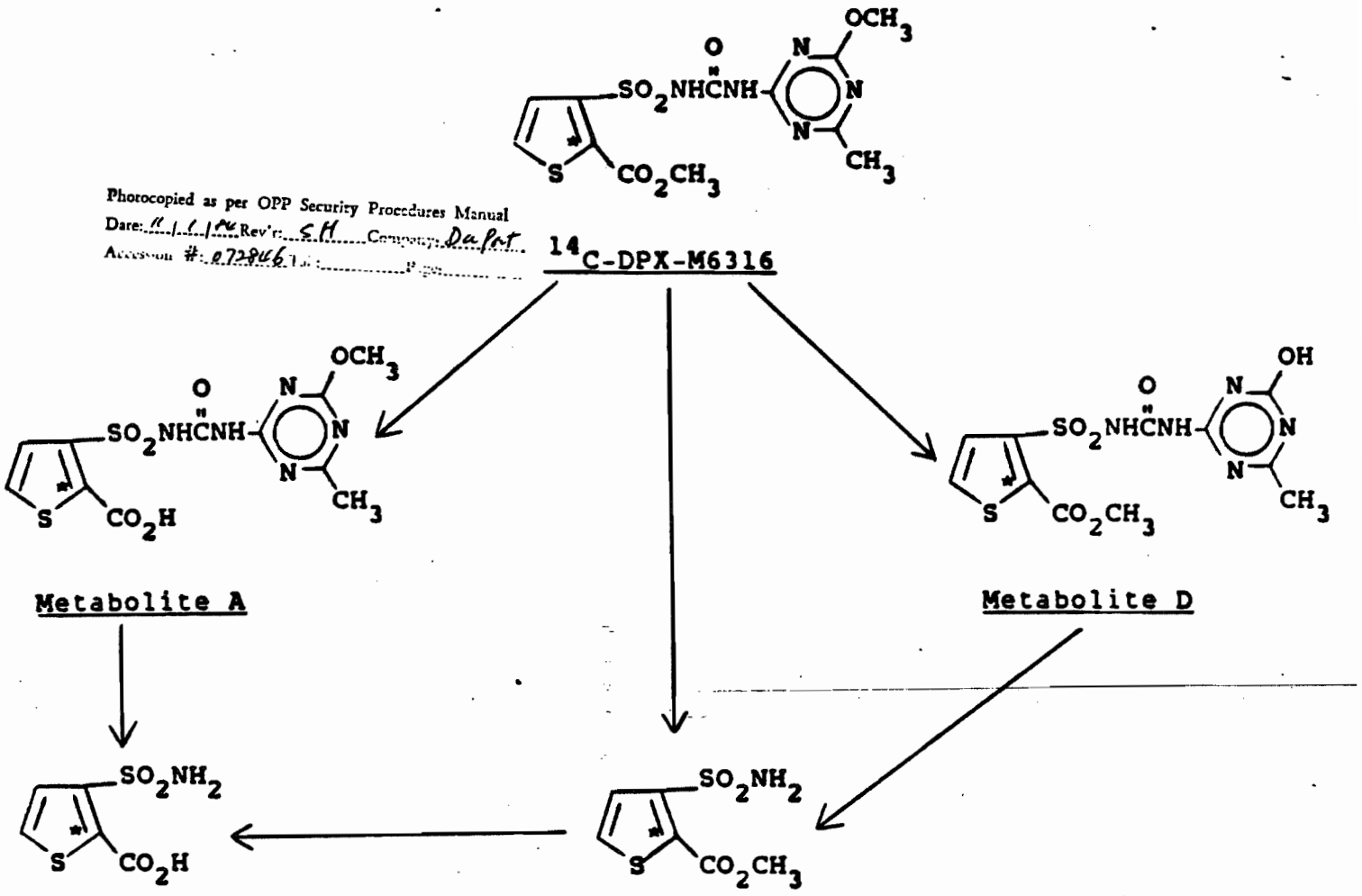
[a] The Flanagan silt loam soils were treated with 51 ppb of DPX-M6316 [thiophene-2-^{14}C] and maintained at 70% of its moisture holding capacity during the incubation at 25°C in the dark.

[b] Structures and Chemical Abstracts names of these compounds are shown in Figure 1.

[c] On the average, ≥99% of the applied radioactivity was recovered.

FIGURE 1

PROPOSED METABOLIC PATHWAY OF DPX-M6316 [THIOPHENE-2-^{14}C] IN AEROBIC SOILS



Met. A: 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]-sulfonyl]-2-thiophenecarboxylic acid

Met. B: (3-aminosulfonyl)-2-thiophenecarboxylic acid

Met. C: methyl 3-(aminosulfonyl)-2-thiophene-Carboxylic acid

Met. D: methyl 3-[[[[(4-hydroxy-6-methyl-],3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl 2-thiophenecarboxylic acid

Met. E: thieno[2,3-d]isothiazole-3(2H)-one, ~~1,1-dioxide~~

* Denotes location of ^{14}C label.

Conclusion

DPX-M6316[thiophene-2-^{14}C] was metabolized to $^{14}CO_2$ via several degradation intermediates (figure 1) with a half-life of 2-6 days under the experimental conditions. Thirty-one to 44 % of the applied ^{14}C (in thiazole ring) was mineralized after 20 weeks of incubation.

3.2.2 Microbial Degradation of ^{14}C-DPX-4189 in Soil. C. Rapisarda, Undated, Du Pont Document No. AMR-43-81.

This study was previously reviewed in connection with DPX-T6376 (ALLY®, EAB review dated 7/12/84) registration. It was concluded that this study adequately addressed the fate of triazine moiety of the compound in soil.

Since the triazine moiety in DPX-6316 is the same as in DPX-4189 and DPX-T6376, the fate of the triazine moiety of DPX-M6316 in soil will be the same as that of DPX-4189.

3.3 Residue Accumulation in Rotational Crops

3.3.1 Crop Rotation Study with ^{14}C-DPX-W4189. J. C-Y. Han, Undated, Du Pont Document No. AMR-46-81.

This study has EPA Accession No.070470 from the previous submission, but EAB file revealed no record of the review of the study.

Experimental

Spring wheat was planted (2nd week of April, 1979) on two Keyport silt loam plots (12 ft^2 each, soil characteristics, table 1). When the seedlings were about 8-10" high with fourth leaf fully expanded, one plot was uniformly treated with [^{14}C-phenyl]DPX-W4189 at 70 g/ha and the other was treated with [^{14}C-triazine]DPX-W4189 (figure 1). Mature wheat was harvested in July 1979.

Next spring, sugar beets, rape and soybeans were planted on both ^{14}C-treated plots (5/30/80).

Sugar beets died within a month after germination. Rape and soybeans were also slightly injured, but both of these crops recovered after 3 weeks.

Mature soybeans (beans and foliage) and rape foliage were harvested in November 1980. After winter dormancy, rape resumed growth in 1981 and seeds and foliage at maturity (6/30/81) were collected for analysis.

Soil core samples (3/4 x 12") were taken at planting and every harvest.

Section 3.3.1

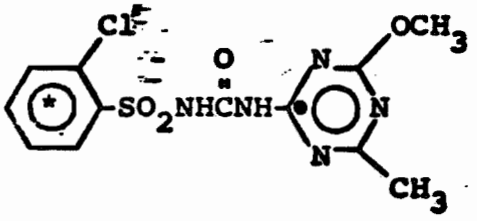
Table I

Characteristics of Keyport Silt Loam

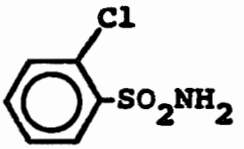
(Analyzed by Soil Testing Laboratory, University of Delaware)

pH	6.0
Mg	105
P_2O_5	46
K_2O	39
Ca	104
Sand USDA (2.0-0.05 mm)	16.2
ISSS (2.0-0.02 mm)	40.3
Silt USDA (0.05-0.002 mm)	72.8
ISSS (0.02-0.002 mm)	48.7
Clay (<0.002 mm)	11.0
Textural Class, USDA	Silt loam
ISSS	Loam
Cation Exchange Capacity (meq/100 g)	7.73
Organic Matter	1.4%

Chemical Structures Of DPX-W4189 And Possible Metabolites/Degradation Products

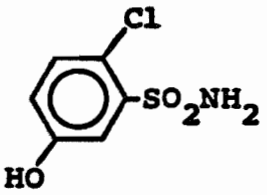


DPX-W4189
2-chloro-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminocarbonyl]-benzenesulfonamide



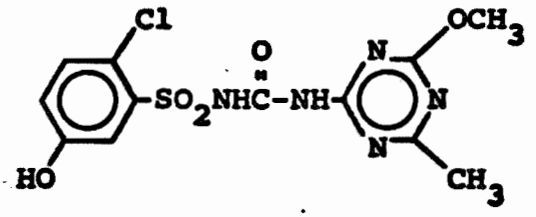
2-chlorobenzenesulfonamide

(I)



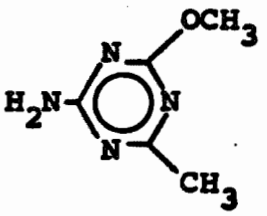
2-chloro-5-hydroxy-benzenesulfonamide

(II)



2-chloro-5-hydroxy-N-[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)aminocarbonyl]-benzenesulfonamide

(III)



2-amino-4-methoxy-6-methyl-1,3,5-triazine

(IV)

* denotes position of label in phenyl labeled DPX-W4189

• denotes position of label in triazine labeled DPX-W4189

The total ^{14}C was measured by combustion analysis after soil and seeds were air-dried and homogenized and after foliage was chopped into small pieces.

Plant tissue samples were extracted in a blender with acetone/water (8/2), centrifuged, and the supernatant was reduced to a small volume. The concentrated extract was adjusted to pH 3 with 1 N H_2SO_4 and extracted with ether (2x). The ether extract was evaporated to dryness under nitrogen. The remaining aqueous layer was reextracted with n-butanol (2x) and the n-butanol evaporated. Then ether and n-butanol fractions were analysed by TLC in toluene/acetone (1/1) and CH_3CN/EtOAc/HCOOH (150/50/1.5) with standard compounds.

An aliquot of soil samples was refluxed with 5 % $(NH_4)_2CO_3$ in methanol/water (2:1) and then cooled and centrifuged. The supernatant and methanol wash of the soil residue were combined and boiled gently on a hot plate to evaporate and decompose ammonium carbonate. The concetrate was partitioned with a mixture of water and ethyl acetate. After radioassay, both phases were concentrated and analyzed by TLC in toluene/acetone (1:1).

Results

In all soil analyses parent compound was found to be 1 ppb or less (table 2). ^{14}C-2-Chlorobenzenesulfonamide and ^{14}C-2-amino-4-methoxy-6-methyl-1,3,5-triazine were found to be 3 ppb and 4 ppb, respectively after 1 year of aging but these were found to be 1 ppb after 1.5 years and less than 1 ppb after 2 years.

^{14}C-Residues in plant tissues of rotational crops are shown in table 3. Dry soybean foliage had a total ^{14}C-residue of between 7 and 9 ppb, calculated as intact DPX-W4189. Beans had a total residue of 2-3 ppb. After the first growing season, 3-4 ppb was found in dry rape foliage and ^{14}C-residue decreased to 2 ppb at maturity in the second growing season. Rape seeds had 1 ppb from both labeled treatments. Extraction analyses showed that less than 1 ppb was found in all fractions from all tissue samples except in water phase from the soybean foliage where 3 ppb was found from both treatments.

Comments

A number of deficiencies found in this study include:

- Rotational crops should include those expected to be representative of roots, small grains and leafy vegetables. No studies with small grain or root was done.
- Residue analysis in the soil at the time of treatment was not done.

Section 3.3.1

Table 2

Residues in Soil From Treatment of ^{14}C-Labeled DPX-W4189

(Treatment Rate 70 g/ha)

-Label tion	Crop	Months After Treatment: Aging Period At Planting	Radioactive Residue (Calculated as ^{14}C-DPX-W4189: Total ^{14}C In Soil	^{14}C-DPX-W4189	^{14}C-2-chloro-benzenesulfonamide	^{14}C-2-amino-4-methoxy-6-methyl-1,3,5-triazine
yl	None (Soil)	12	27 ppb	1 ppb	3 ppb	---
zine	None (Soil)	12	29 ppb	1 ppb	---	4 ppb
		Aging Period At Harvest				
yl	Soybean	18	18 ppb	<1 ppb	1 ppb	---
zine	Soybean	18	15 ppb	<1 ppb	---	1 ppb
yl	Rape	25	10 ppb	<1 ppb	<1 ppb	---
zine	Rape	25	10 ppb	<1 ppb	---	<1 ppb

Section 3.3.1.1

Table 3

^{14}C-Residues in Rotational Crops Grown on Soil Previously Treated With ^{14}C-DPX-W4189

^{14}C-Phenyl-Labeled DPX-W4189 Treatment	ppb ^{14}C-Residue (Calc'd. as DPX-W4189)			
	Total	Ether Phase	n-butanol Phase	Water Phase
Dry Soybean Foliage	9	<1	<1	3
Edible Soybean	3	<1	<1	<1
Rape Foliage (End of the 1st Growing Season)	3	<1	<1	1
Rape Foliage (Mature Stage)	2	<1	<1	<1
Rape Seed	1	<1	<1	<1
^{14}C-Triazine-Labeled DPX-W4189 Treatment				
Dry Soybean Foliage	7	<1	<1	3
Edible Soybean	2	<1	<1	<1
Rape Foliage (End of the 1st Growing Season)	4	<1	<1	1
Rape Foliage (Mature Stage)	2	<1	<1	<1
Rape Seed	1	<1	<1	<1

- The treatment rate used in this study, 70 g/ha, is only one-half of the maximum treatment rate (2 oz/a, 140 g/ha) in the label: Even after one-year of aging with one-half of the maximum application rate, DPX-4189 residues (27 ppb among which only 1 ppb was parent compound) showed fatal toxicity to sugar beet seedlings. Also, it produced slight injury in soybeans and rape. If the maximum rate had been used, all of the crops might have died. Also, the soil concentration and the tissue concentration would have been higher.

- No rainfall data, temperature monitoring data and general climatic conditions were reported for the test period.

This study does not satisfy the rotational crop data requirement on DPX-4189. Moreover, the rotational crop data requirement on DPX-M6316 cannot be supported by the studies done with DPX-4189 since the rate of metabolism, metabolites produced in soil and the application rate are different from each other.

3.3.2 Crop Rotation Study with ^{14}C-DPX-T6376 in the Greenhouse. J. Harvey, Jr., Undated, Du Pont Document No, AMR-120-83.

Experimental

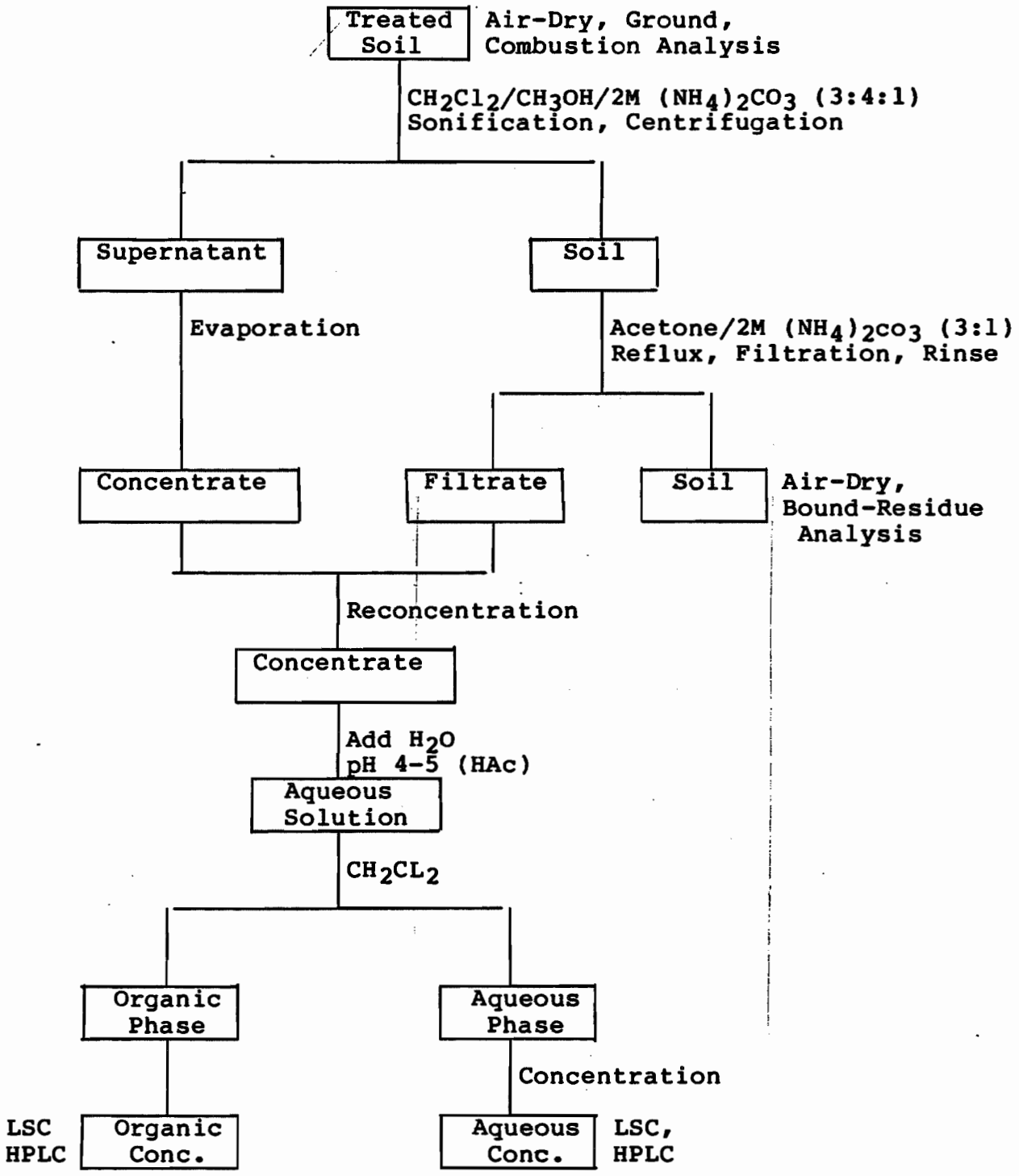
Common clay flower pots (16-inch i.d., surface area 0.113 m^2, volumn 0.75 ft^3 = 0.021 m^3) were filled to within 1 inch of the rim with a Woodstown sand loam soil (USDA sand 58 %, silt 36 %, clay 6 %, CEC 5.2 %, O.M. 1.4 %, pH 4.9). The surface of the soil in each pot was treated with a solution of [^{14}C-phenyl]-DPX-T6376 (24.8 uCi/mg, 98.4 % radiopurity) in acetone at 0.177 mg (9.54×10^6 dpm)/pot (equivalent to 16 g/ha). The treated soil was watered to maintain the soil moisture while aging for 120 days under greenhouse conditions.

At the end of the aging period, sugar beets, rape and oats were seeded. Twenty days later, soybeans were seeded. These crops were allowed to grow under ambient greenhouse conditions with supplemental fluorescent lighting to maintain day length at 14 hours.

Soil samples were taken at planting and 70 and 172 days after planting. Plant tissue samples were taken 35 and 70 days after planting and at maturity.

Selected plant tissues from mature crops were extracted with acetone/water (8:2) (3x), the extracts concentrated, acidified and extracted with CH_2Cl_2 (3x) and then n-butanol. The extracted tissue was air-dried and radioassayed. A Zorbax® C8 HPLC column was used with mobile phases of 36 % CH_3CN in pH 2.2 water (H_3PO_4) for CH_2Cl_2 concentrates and 40 % CH_3CN for aqueous concentrates.

Soil samples were analyzed according to the following scheme.



Results

The soil residues are shown in the following table.

	Aging (day)		
	120(planting)	120 + 70	120 + 172
Total ^{14}C (ppb)	1.2	1.3	0.9
Identified residues			
DPX-T6376	0.12		<0.02
Methyl(amino sulfonyl)benzoate	0.06		--
Saccharin	0.05		0.10
2-(Aminosulfonyl)-benzoic acid	0.01		0.05
Bound residue	0.48		--

The ^{14}C-residues in plant tissue are shown in the following table.

	^{14}C-Residue calculated as ppb		
Crop	30 days after planting	71 days after planting	matirity
Sugar beets			
Foliage	< 1	2	2
root	-	-	1
Rape			
Foliage	10	-	4
Seed	-	-	3
Oats			
Foliage	10	-	8*
Grain	-	-	2*
Soybeans			
Floiage	10**	3***	41
Beans	-	-	2

* Calculated on a dry weight basis. All other data are calculated on a fresh weight basis.
** 22 Days after planting.
*** 50 Days after planting.

The ^{14}C-residue distribution in mature soybean foliage and seeds is shown in the following table.

	Conc. of ^{14}C-Residue Calculated as ppb DPX-T6376	
	Foliage	Seeds
Total ^{14}C	41	2
CH_2Cl_2 Soluble	27	0.5
Butanol Soluble	6	1.1
Water Soluble	5	0.3
Unextractable	3	0.1

It was reported that DPX-T6376 represented less than 0.3 ppb in the CH_2Cl_2 soluble from both foliage and seeds.

Comments

A number of deficiencies were found in the study.

- o Material balance and zero time data (right after treatment) were not reported in soil analyses.
- o Recoveries were not reported.
- o Actual concentration of individual metabolites in rotational crops was not reported. It was reported that DPX-T6376 represented less than 0.3 ppb in CH_2Cl_2 fraction from both soybean foliage and seeds. No TLC/LSC analysis was done, which might have provided the concentration of parent compound and metabolites as well.
- o This study does not provide any information about residue accumulation from the triazine moiety of the molecule.

Conclusion

This study does not satisfy the rotational crop data requirement for DPX-T6376 and/or DPX-M6316.

Recommendations

To support the rotational crop data requirement for DPX-T6376, the individual concentrations of parent and metabolites need to be determined.

To support the rotational crop data requirement for DPX-M6316, a separate study using DPX-M6316 needs to be done.

3.3.3 Crop Rotation Study with ^{14}C-Metsulfuron Methyl in the Field. J. J. Anderson, Undated, Du Pont Document No. AMR-190-84.

Experimental

A plot (5 x 5 m) of winter wheat in the boot stage was treated (5/21/82) with metsulfuron methyl[^{14}C-phenyl] (8.62 uCi/mg, 99 % radiopurity) at a rate of 30 g/ha and all the treated wheat was removed within 3 weeks.

The following spring, after the plot was tilled to a depth of 6-8 inches, oats, soybeans, rape and sorghum were planted (5/18/83). Red beets were planted on 7/9/83 and 7/12/83.

Soil samples (10 soil core samples) were taken just before planting and after harvesting. Five-gram aliquots of each

soil sample were removed and analyzed for the total radioactivity. Analysis of soil was done by the similar procedure described in section 3.3.2.

Plant samples were removed from the plot at selected intervals up to and including maturity. After weighing, the entire plant sample was lyophilized and ground. Seeds were separated from the straw in mature plant samples. The total ^{14}C residue was measured by combustion analysis.

Aliquots of the dried plant material were ultrasonifically extracted with acetone/water (8:2) (3x). After the extracts were reduced to dryness, the residues dissolved in water (pH 3, phosphoric acid), extracted with CH_2Cl_2. The organic and aqueous fractions were radioassayed.

Results

Soil contained 2 ppb total radiolabeled residues before planting and 1 ppb after all plant samples were removed.

Table 1 shows the total ^{14}C-residue in rotational crops. The % distribution of radioactive residues is shown in table 2.

In general, the ^{14}C-residue level in the tissues of the rotational crops was higher than that in the soil. Rape seeds contained the highest level of radioactive residue (31 ppb).

It was reported that it was impossible to isolate sufficient quantities for identification of individual metabolites.

Comments

Since individual metabolites were not identified and quantitated, the data in tables 1 and 2 cannot adequately describe the actual accumulation in rotational crops. The author explained that it was impossible to isolate the metabolites. However, no description was made what methodology was used (it seems likely that HPLC was employed). TLC separation and subsequent quantitation by LSC might be able to identify and quantitate metabolites.

No rainfall or irrigation data were provided.

Other comments in section 3.3.2 stand.

Section 3.3.3

TABLE 1

RADIOACTIVE RESIDUES IN PLANT TISSUE AS A FUNCTION OF TIME[a]

Crop	Portion	Sampling Date[b]	Parts Per Billion Total Radioactivity[c]
Oats	Foliage	7/21	2
	Straw	8/12[d]	9
	Grain	8/12[d]	8
Rape	Foliage	7/21	9
	Foliage	8/12	4
	Straw	8/26[d]	5
	Seed	8/26[d]	31
Soybeans	Foliage	7/21	4
	Foliage	8/12	4
	Foliage	8/26	1
	Foliage	9/9	3
	Foliage	11/7[d]	4
	Bean	11/7[d]	2
Sorghum	Foliage	7/21	3
	Foliage	8/12	4
	Foliage	8/26	4
	Straw	9/22[d]	4
	Grain	9/22[d]	2

[a] Soil contained 2 ppb total radiolabeled residues before planting and 1 ppb after all plant samples were removed.

[b] Crops were planted on 5/18.

[c] Calculated as metsulfuron methyl.

[d] Maturity date of crop.

Section 3.3.3

TABLE 2

DISTRIBUTION OF RADIOACTIVE RESIDUES IN SOIL AND MATURE PLANT EXTRACTS

Crop	Fraction	Percent of Total Radioactivity		
		H_2O Soluble[a]	CH_2Cl_2 Soluble[b]	Unextracted[c]
Rape	Seed	31	35	34
	Straw	35	33	32
Soybean	Seed	19	27	54
	Foliage	16	55	29
Sorghum	Seed	2	43	55
	Straw	4	44	51
Oats	Seed	<1	8	92
	Straw	4	79	16
	Soil	17	68	16

a Radioactivity remaining in the pH 3 aqueous phase after multiple extractions with methylene chloride.

b Radioactivity extracted from the pH 3 aqueous phase into methylene chloride.

c Radioactivity not extracted by 80% acetone/20% water (for the crop samples) or methylene chloride/methanol/2M $(NH_4)_2CO_3$ (3/4/1, v/v/v) for the soil sample.

3.4 Fish Accumulation

3.4.1 DPX-M6316[Thiophene-2-^{14}C] Flow-Through Bioconcentraion Study with Bluegill Sunfish. J. C. Larkin, Biospherics Incorporated for Du Pont, July 1984, Du Pont Documnet No. AMR-182-84.

Experimental

Bluegill sunfish (average weight 1.67 g, 0.6-3.76 g) were introduced into three glass aquaria (90 x 30 x 40 cm, 108 liter capacity) holding 72.9 liters of water. Two of the aquaria were fortified with DPX-M6316[thiophene-2-^{14}C] at a nominal concentration of 5 ppm by delivering a diluted radioactive stock solution into the system using monostat injector system. The diluted radioactive solution was made by mixing 8 ml of radioactive stock solution (5 mg/ml, 23.1 uCi/mg) with 992 ml of non-labeled DPX-M6316 solution (5 g/L). For each cycle of the diluter system, 4 ml of the diluted radioactive solution was ultimately diluted to 4 liters. A third aquarium served as a control. Water was delivered to both control and test chambers by a diluter system as diagrammed schematically in figure 1. A summary of test parameters is presented in table 1.

A total of 80 fish were added to each tank with removal of 4 fish (2 for dissection and 2 for whole fish analysis) and 5 ml water on days 0, 1, 3, 10, 14, 21 and 28. Control fish were sampled on days 0, 1, 14 and 28. During depuration, fish were sampled on days 1, 3, 7, 10 and 14. Control fish were sampled on day 14.

Water samples (5 ml) were analyzed by LSC. Tissue samples were analyzed by combustion analysis.

The estimated sensitivity of detection with a 1.17 g tissue sample was about 3.7 ppm and the minimum detectable concentration for 5.0 ml water sample was about 0.9 ppm.

Results

No mortality was observed during the entire study period from both test and control chambers.

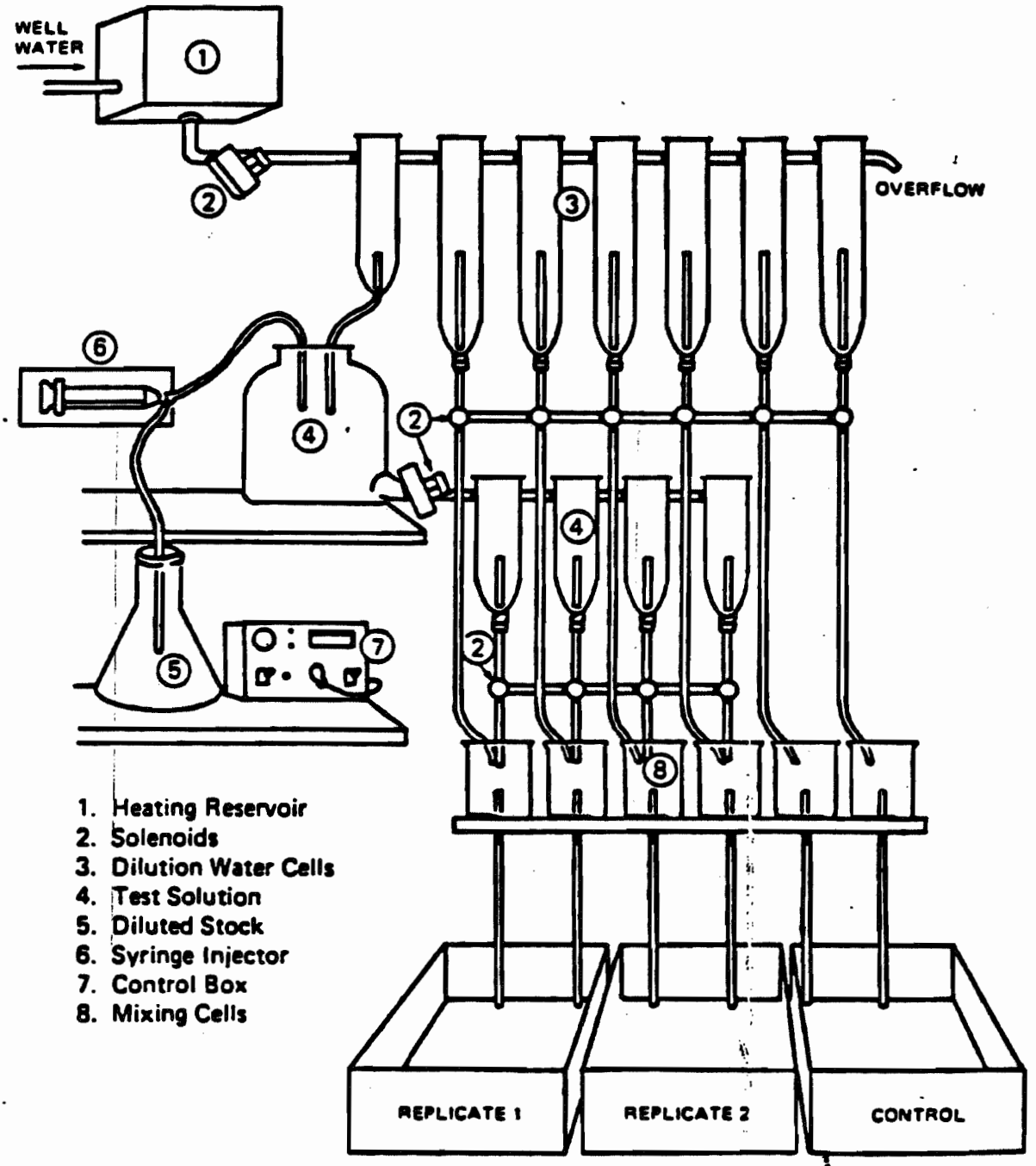
Results from the analysis of water samples are shown in table 2. The average water concentration of DPX-M6316 [thiophene-2-^{14}C] was 4.4 ppm during the exposure phase and < 0.9 ppm during the depuration phase.

Results from the analysis of fish samples are shown in tables 3 and 4. Throughout the study, no bioaccumulation of ^{14}C residues from DPX-M6316[thiophene-2-^{14}C] occurred in bulegill sunfish.

Section 3.4.1

Figure 1.

Schematic of Bluegill Bioconcentration System



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DPX-M6316 [thiophene-2-^{14}C] Bluegill Sunfish Bioconcentration Study
Summary of Test Parameters

Parameter	Measurement, Setting or Condition
1. Test material & source.	1. DPX-M6316 [thiophene-2-^{14}C] (Specific Activity = 23.1 µCi/mg) was [redacted] supplied by the DuPont Agricultural Chemicals Department under the code ^{14}C-H-15,150.
2. Test type.	2. Flow-through, bluegill sunfish bioconcentration.
3. Test phases & durations	3. Uptake (28 days) and depuration (14 days).
4. Physical test apparatus.	4. Solenoid Activated Diluter System, Aquatic Toxicology Flow-through Bioconcentration Apparatus, (Figure 1).
5. Test compound stock solution concentration.	5. 5.0 mg/mL in well water (pH adjusted to 11).
6. Nominal concentration of test compound in the exposure well water.	6. 4.4 parts per million.
7. Test chambers.	7. Three, 90 cm x 30 cm x 40 cm all-glass aquaria, maximum volume 108 liters, water volume 72.9 liters.
8. Exposure and depuration water.	8. Biospherics Laboratory well water, 2 liter/tank/cycle. Total hardness 108 mg/L as $CaCO_3$, total alkalinity 152 mg/L as $CaCO_3$, pH 7.0-7.4, temperature 21 ± 1°C, O_2 concentration 7.2 ± 0.2 (1s) mg/L, specific conductance 360 µmhos/cm.
9. Photoperiod.	9. 16 hrs light/24-hr cycle during both the exposure and depuration phases.
10. Bioassay organism.	10. Bluegill sunfish, Lepomis macrochirus, average weight 1.67 g, initial no./tank 80. Static loading rate 1.83 g/L.
11. Mortality determinations.	11. Direct visual observations.
12. Radiometric analyses	12. ^{14}C determinations in water and fish tissues.

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Section 3.4.1

TABLE 2

DPX-M6316 [thiophene-2-^{14}C] Bluegill Sunfish Bioconcentration Study
Concentration of ^{14}C (Expressed as ppm DPX-M6316)
in Exposure Water

Concentration in ppm and Standard Deviation

	Sampling Date I.D.[a]		Replicate 1		Replicate 2		Average	
			ppm	Std. Dev.	ppm	Std. Dev.	ppm	Std. Dev.
Exposure	0	0	3.2	0.1	3.2	0.1	3.2	0.1
	1	1	3.2	0.1	3.4	0.2	3.3	0.2
	3	3	5.0	0.1	5.0	0.1	5.0	0.1
	7	7	5.4	0.6	5.5	0.2	5.4	0.4
	10	10	4.8	0.1	4.8	0.1	4.8	0.1
	14	14	4.4	0.3	4.5	0.2	4.4	0.2
	21	21	4.8	0.1	4.4	0.5	4.6	0.4
	28	28	4.4	0.2	4.6	0.2	4.5	0.2
Depuration	29	01	<0.9		<0.9		<0.9	
	31	03	<0.9		<0.9		<0.9	
	35	07	<0.9		<0.9		<0.9	
	38	010	<0.9		<0.9		<0.9	
	42	014	<0.9		<0.9		<0.9	

[a]I.D. - consists of 2 columns

First Column - the total number of days that the study had been running since test initiation.
Second Column - the number of days of fish exposure or depuration.

Maximum Percent Counting Error = 5.2 %

Table 3

Concentration of ^{14}C (Expressed as ppm DPX-M6316) and Bioconcentration Factors in Edible and Nonedible Tissues

	Sampling Date I.D.[b]		Edible Fish Tissue ppm			Edible Fish Tissue Bioconcentration Factor (BCF)			Nonedible Fish[a] Tissue ppm			Nonedible Fish[a] Tissue Bioconcentration Factor (BCF)[c]		
			Rep 1	Rep 2	Avg	Rep 1	Rep 2	Avg	Rep 1	Rep 2	Avg	Rep 1	Rep 2	Avg
Exposure	0	0	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	1	1	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	5.3	<3.7	4.5	1.2	<0.8	1.0
	3	3	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	7	7	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	10	10	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	14	14	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	21	21	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	28	28	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
Depuration	29	1	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	31	3	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	35	2	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	38	10	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	42	14	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8

[a] All data from nonedible tissue combustions were less than the detection limit of 3.7 ppm except day 1 (4.5 ppm). Mean water concentration in the treated aquaria for the 28-day exposure period was 4.4 ppm.

[b] I.D. consists of 2 columns:
First Column - the total number of days the study has been running since test initiation.
Second Column - the number of days of fish exposure or depuration.

[c] BCF Detection limit = 0.8

Maximum Percent Counting error = 5.57 %

Section 3, 4.1

Table 4

Concentration of ^{14}C (Expressed as ppm DPX-M6316) and Bioconcentration Factors in Whole Fish Tissue

Whole Fish[a]

	Sampling Date		ppm			Bioconcentration Factor (BCF)[c]		
	I.D.[b]		Rep 1	Rep 2	Avg	Rep 1	Rep 2	Avg
Exposure	0	0	<3.7	4.2	4.0	<0.8[c]	1.0	0.9
	1	1	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	3	3	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	7	7	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	10	10	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	14	14	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	21	21	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	28	28	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
Depuration	29	1	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	31	3	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	35	7	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	38	10	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8
	42	14	<3.7	<3.7	<3.7	<0.8	<0.8	<0.8

[a] All data from whole fish combustions were less than the detection limit of 3.7 ppm except day 0 (4.0 ppm). The mean water concentration of DPX-M6316 treated aquaria water for the 28 day uptake period was 4.4 ppm.

[b] I.D. consists of 2 columns:
First Column - the total number of days the study has been running since test initiation.
Second Column - the number of days of fish exposure or depuration.

[c] BCF Detection Limit = 0.8

Conclusion

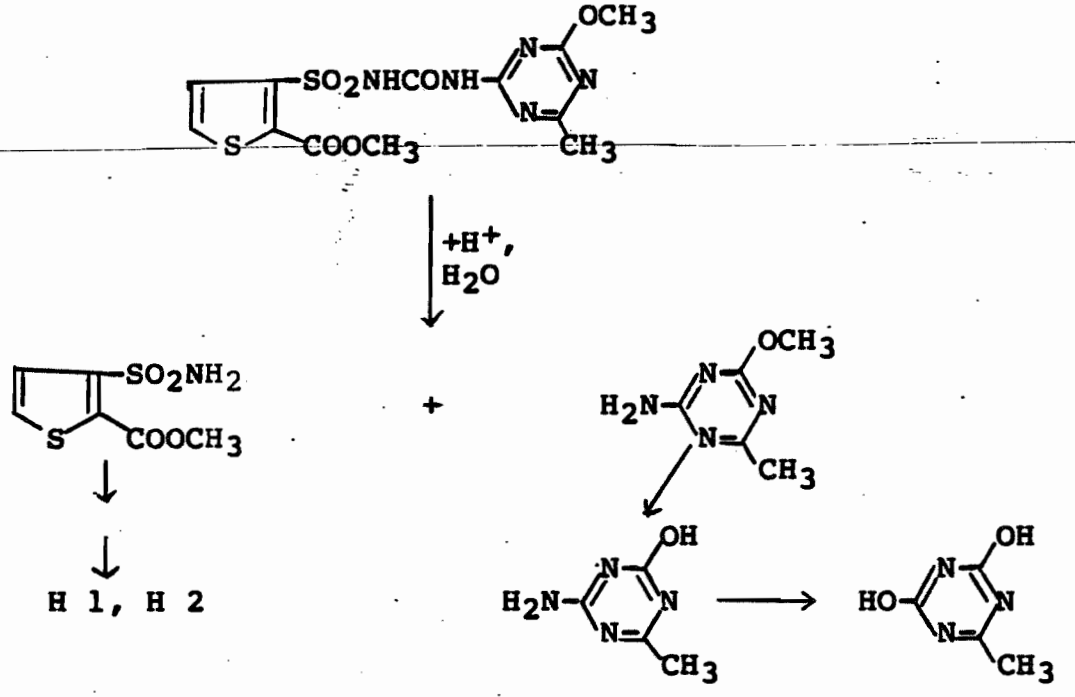
DPX-M6316 appears not to bioaccumlate in bluegill sunfish under flow-through conditions.

This study was well done and satisfies the fish accumulation data requirement.

4.0 EXECUTIVE SUMMARY

4.1 Hydrolysis

DPX-M6316 appears to be relatively stable under neutral to basic conditions but it is hydrolysed under acidic conditions to give methyl 3-(aminosulfonyl)-2-thiophene-carboxylic acid [thiazole ring moiety] and 2-amino-4-methoxy-6-methyl-1,3,5-triazine [triazine ring moiety] with a half-life about 4-6 days at pH 5. The thiazole moiety seems to undergo further degradation to produce the unkown compounds, H 1 and H 2, while the triazine moiety is relatively stable with little degradation (<2 %) to corresponding hydroxy compounds.



However, the hydrolysis data requirement for DPX-M6316 is not satisfied because the unknown product, H 1 which accounted for about 35 % after 21 days of hydrolysis at pH 5 was not identified.

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4.2 Aerobic Soil Metabolism

DPX-M6316 was mineralized to CO_2 in soil. Both thiazole and triazine moieties are susceptible to mineralization.

Five intermediate metabolites were found (figure 1 in section 3.2.1) from thiazole-labeled parent compound. The half-life was estimated to be 2-6 days. After 20 weeks of incubation, 31-44 % of the applied ^{14}C was mineralized and 23-38 % was bound to soil.

The triazine moiety produced after hydrolysis of DPX-M6316 is predicted to be metabolized to the same products found in hydrolysis studies (see section 4.1) since those metabolites were found in the soil metabolism study done with DPX-4189-[thiazoine-^{14}C].

Data requirement for the aerobic soil metabolism on DPX-M6316 is satisfied.

4.3 Rotational Crops

No data obtained from the study done with DPX-M6316 were submitted. Data submitted were obtained from the studies with either DPX-W4189 (chlorsulfuron) or DPX-T6376 (metsulfuron methyl) and are considered inadequate.

4.4 Fish Accumulation

DPX-M6316 appears not to bioaccumulate (BCF <0.8) in bluegill sunfish under flow-through conditions.

Fish accumulation data requirement is satisfied.

5.0 CONCLUSION AND RECOMMENDATION

5.1 The following environmental fate data requirements have been satisfied for DPX-M6316:

- o Aerobic soil metabolism
- o Fish accumulation
- o Hydrolysis (for <u>EUP only</u>: To satisfy the data requirement for full registration, the unknown product, H 1, needs to be identified.)

5.2 Rotational crop studies need to be done with DPX-M6316. Without the results of rotational crop studies, the proposed labeling (30 days of restriction for DPX-M6316 and 120 days for DPX-M6316 plus Ally® tank mix) cannot be assessed as adequate. In spite of the low application rate and short half-life of DPX-M6316, complete rotational crop studies

will be needed to set a rotational crop restriction. In lieu of rotational crop studies, a statement not allowing rotation to the treated fields on the label will be acceptable. The proposed rotational crop restriction of 30 days is not adequate in light of the crop injury noted to occur 12 months after use of DPX-4189.

5.3 In the aerobic metabolism study discussed in section 3.3.1, the report says that "all flasks were opened weekly to add oxygen to the system". We would like the following questions answered:

- How long were the flasks open to let in O_2?
- Why was there not any loss of volatile ^{14}C?

Soobok Hong

Soobok Hong, Ph.D.
November 1, 1984
Environmental Chemistry Review Section 1
Exposure Assessment Branch/HED

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DPX M6316

HERBICIDE
DRY FLOWABLE

DIRECTIONS
FOR
TRIAL USE

FOR EXPERIMENTAL USE ONLY
EPA EXPERIMENTAL USE PERMIT NO 352-EUP-XXX
IT FOR SALE TO ANY PERSON OTHER THAN A PARTICIPANT OR
PERATOR OF THE EPA-APPROVED EXPERIMENTAL USE PROGRAM

DPX M6316 HERBICIDE DRY FLOWABLE

IVE INGREDIENT:
hyl 3-[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]-
ionyl]amino]sulfonyl]-2-thiophenecarboxylate..... 75%
IT INGREDIENTS 25%
atent (Pending) EPA Est. 352-DE-1

EP OUT OF REACH OF CHILDREN

RECAUTIONARY STATEMENTS
HAZARDS TO HUMANS

ARNING! CAUSES EYE IRRITATION. DO NOT GET IN EYES.

d contact with skin, eyes, and clothing. In case of act with eyes, immediately flush with plenty of water. medical attention if irritation persists. Wash thoroughly handling. Remove and wash contaminated clothing re reuse.

ENVIRONMENTAL HAZARDS

not apply directly to any body of water. Do not aminate water by cleaning of equipment or disposal asles.

IMPORTANT

lo or loss of desirable trees or vegetation may result ilure to observe the following: Do not apply or drain or quipment on or near desirable trees or other plants, or as where their roots may extend, or in locations where emical may be washed or moved into contact with ots. Do not use on lawns, walks, driveways, tennis or similar areas. Prevent drift of spray to desirable Do not contaminate any body of water.

ghly clean all traces of DuPont DPX M6316 Herbi- om application equipment immediately after use. up procedures are described in the "SPRAYER UP" section of this label. Failure to follow these ures may result in injury to subsequently sprayed

STORAGE AND DISPOSAL

STORAGE: Store product in original container only, away from other pesticides, fertilizer, food or feed. Not for use or storage in or around the home. Keep container closed.

DISPOSAL: Product unused at the end of the Experimental Program should be returned to the DuPont Company via the cooperator's program supervisor. Do not contaminate water, food, or feed by disposal. Waste resulting from the use of this product may be disposed of on site or at an approved waste disposal facility. Emptied containers should be triple-rinsed (or equivalent) and offered for recycling or reconditioning or punctured and disposed of in a sanitary landfill or by other procedures allowed by state and local authorities.

NOTICE OF WARRANTY

This product is for experimental use only. DuPont makes no warranties of merchantability or fitness for a particular purpose nor any other express or implied warranty except as stated above.

GENERAL INFORMATION

Du Pont DPX M6316 Herbicide is recommended for trial use for selective postemergence control of broadleaf weeds in wheat (including durum) and barley. DPX M6316 is a dry flowable granule to be mixed in water and applied as a uniform broadcast spray. It is noncorrosive, nonflammable, nonvolatile, and does not freeze.

Best results are obtained when DPX M6316 is applied to young actively growing weeds. The rate used will depend on weed spectrum and size of weed at time of application. The degree of control and duration of effect are dependent on rate used, sensitivity and size of target weed, and growing conditions at the time of application.

Trials have shown that DPX M6316 stops growth of susceptible weeds rapidly. However, typical symptoms (discoloration) of dying weeds may not be noticeable for 1 to 3 weeks after application depending on growing conditions and weed susceptibility. Warm, moist conditions following treatment promote the activity of DPX M6316 while cold, dry conditions delay the activity. Weeds hardened off by cold weather or drought stress will be less susceptible.

Continued on back side

DIRECTIONS FOR TRIAL USE

It is a violation of federal law to use this product in a manner inconsistent with its labeling.

DPX M6316 should be used only in accordance with recommendations on this label or in separate published DuPont recommendations.

DuPont will not be responsible for losses or damages resulting from the use of this product in any manner not specifically recommended by DuPont.

RATES FOR TRIAL USE

Apply 1/6 to 1-1/3 ounces of DPX M6316 per acre postemergence to wheat (including durum) or barley to evaluate control or suppression of emerged:

- Fiddleneck (Tarweed)
- Field pennycress
- Flixweed
- Gromwell
- Jim Hill mustard
- Kochia
- Lambsquarters
- Redroot pigweed
- Russian thistle
- Sunflower
- Treacle mustard
- Wild buckwheat
- Wild garlic
- Wild mustard

Note: If rain occurs within 8 hours of application, control may be reduced.

TIMING OF APPLICATION

Spring Cereals: Apply any time after the crop is in the 2-leaf stage but before "boot" stage.

Winter Cereals: Apply any time the crop is actively growing between the 2-leaf and "boot" stage.

For best results apply to emerged weeds that are less than 4" tall or across and before the crop canopy closes in. Weeds that emerge after treatment will not be controlled.

DPX M6316 Plus Ally™*

DPX M6316 (1/3 to 1-1/3 ounces per acre) plus DuPont Ally™ Herbicide (1/20 to 1/15 ounce per acre) may be applied as a tank mixture to evaluate the control or suppression of broadleaf weeds. Application timing of this tank mixture should correspond to that of DPX M6316 alone.

EQUIPMENT — SPRAY VOLUMES

Apply uniformly using properly calibrated air or ground equipment. Use at least 1 gallon spray volume per acre by air or 5 gallons per acre by ground. Use 50-mesh screens or larger.

Continuous agitation is required to keep DPX M6316 in suspension. Avoid overlapping, and shut off spray booms while starting, turning, slowing or stopping, or injury to the crop may result.

NOTE: Do not allow spray to drift onto adjacent crops as injury to the adjacent crop may occur.

SPRAY PREPARATION/TANK MIXTURES

DPX M6316 may be tank mixed with suitable registered herbicides to control weeds other than those listed. Follow the manufacturer's label for the companion herbicide. If application timing of the companion herbicide differs from that of DPX M6316, do not tank mix.

Mix the proper amount of DPX M6316 into the necessary volume of water in the spray tank with the agitator running. Agitation is required for uniform suspension and application. For tank mixtures, add the companion herbicide next to the spray tank.

To improve wetting and/or contact activity of DPX M6316, a surfactant of at least 80% active ingredient should then be added as the last ingredient at the rate of 1 quart per 100 gallons of spray. Additional surfactant is not needed if it is already included in the companion herbicide formulation.

NOTE: Use DPX M6316 spray mixture within 24 hours of preparation, or product degradation may occur.

SPRAYER CLEANUP

To avoid subsequent injury to crops other than wheat or barley, immediately after spraying thoroughly remove all traces of DPX M6316 from mixing and spray equipment as follows:

1) Drain tank; then flush tank, boom and hoses with clean water for a minimum of 10 minutes.
2) Fill the tank with clean water, then add ½ gallon chlorine bleach (containing 5¼% sodium hypochlorite) per 100 gallons of water. Flush solution through boom and hoses, then allow to sit for 15 minutes with agitation, then drain.
3) Repeat Step 2.
4) Nozzles and screens should be removed and cleaned separately. To remove traces of chlorine bleach, rinse the tank thoroughly with clean water and flush through hoses and boom.

CAUTION: Do not use chlorine bleach with ammonia. All traces of liquid fertilizer containing ammonia, ammonium nitrate or ammonium sulphate must be rinsed with water from the mixing and application equipment before adding chlorine bleach solution. Failure to do so will release a gas with a musty chlorine odor which can cause eye, nose, throat and lung irritation. Do not clean equipment in an enclosed area.

PRECAUTIONS

Do not graze or feed forage or hay from treated areas to livestock.

Do not plant to any crop other than wheat or barley for 30 days after application of DPX M6316.

Do not plant to crops other than wheat or barley for 120 days after the application of DPX M6316 plus Ally™ tank mixtures where the use rate of Ally™ is below 1/15 ounce per acre.

Do not apply to wheat or barley that is stressed by a severe winter, drought, water saturated soil, disease, or insect damage as crop injury may result.

Do not apply to flood or furrow irrigated land where tail water will be used to irrigate crop land.

Do not apply to cereal crops underseeded to legumes as injury to legume forage may result.

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E.I. DU PONT DE NEMOURS & CO. (INC.), AGRICULTURAL CHEMICALS DEPARTMENT, WILMINGTON, DELAWARE 19898

IMPORTANT

Injury to or loss of desirable trees or vegetation may result from failure to observe the following: Do not apply or drain or flush equipment on or near desirable trees or other plants, or on areas where their roots may extend, or in locations where the chemical may be washed or moved into contact with their roots. Do not use on lawns, walks, driveways, tennis courts, or similar areas. Prevent drift of spray to desirable plants. Do not contaminate any body of water.

Thoroughly clean all traces of DuPont DPX M6316 Herbicide from application equipment immediately after use. Clean-up procedures are described in the "SPRAYER CLEAN-UP" section of this label. Failure to follow these procedures may result in injury to subsequently sprayed crops.

STORAGE AND DISPOSAL

STORAGE: Store product in original container only, away from other pesticides, fertilizer, food or feed. Not for use or storage in or around the home. Keep container closed.

DISPOSAL: Product unused at the end of the Experimental Program should be returned to the DuPont Company via the cooperator's program supervisor. Do not contaminate water, food, or feed by disposal. Waste resulting from the use of this product may be disposed of on site or at an approved waste disposal facility. Emptied containers should be triple-rinsed (or equivalent) and offered for recycling or reconditioning or punctured and disposed of in a sanitary landfill or by other procedures allowed by state and local authorities.

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SEE DIRECTIONS FOR TRIAL USE ATTACHED

AG-277 0884

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Printed in U.S.A.

FOR EXPERIMENTAL USE ONLY
EPA EXPERIMENTAL USE PERMIT NO 352-EUP-XXX
NOT FOR SALE TO ANY PERSON OTHER THAN A PARTICIPANT OR COOPERATOR OF THE EPA-APPROVED EXPERIMENTAL USE PROGRAM

DPX M6316
HERBICIDE DRY FLOWABLE

ACTIVE INGREDIENT:

Methyl 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]-sulfonyl]-2-thiophenecarboxylate 75%

INERT INGREDIENTS 25%

U.S. Patent (Pending) EPA Est. 352-DE-1

KEEP OUT OF REACH OF CHILDREN

PRECAUTIONARY STATEMENTS HAZARDS TO HUMANS

WARNING! CAUSES EYE IRRITATION DO NOT GET IN EYES.

Avoid contact with skin, eyes, and clothing. In case of contact with eyes, immediately flush with plenty of water. Get medical attention if irritation persists. Wash thoroughly after handling. Remove and wash contaminated clothing before reuse.

ENVIRONMENTAL HAZARDS

Do not apply directly to any body of water. Do not contaminate water by cleaning of equipment or disposal of wastes.

Net Weight 8 oz

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Harmony Reviews

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___ Description of product quality control procedures

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