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Shaughnessy No. _____

Date out of EAB: 03 NOV 1983

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

From: Richard V. Moraski, Ph.D., Acting Chief
Environmental Chemistry Review Section I
Exposure Assessment Branch
Hazard Evaluation Division (TS-769c)

Attached please find the EAB review of...

Reg./File No.: 8340 - EUP - T

Chemical: HOE 33171

Type Product: Herbicide

Product Name: Whip 1 EC Herbicide

Company Name: American Hoechst

Submission Purpose: EUP on soybeans

ZBB Code: other

ACTION CODE: 710

Date In: 8/15/83

EFB # 3493

Date Completed: 10/31/83

TAIS (level II) 52 Days 9

Deferrals To:

_____ Ecological Effects Branch

_____ Residue Chemistry Branch

_____ Toxicology Branch

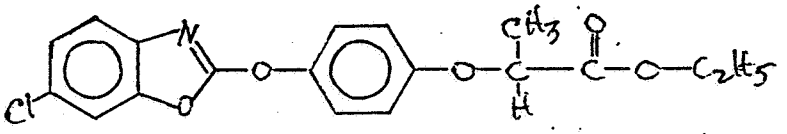
1.0 INTRODUCTION

Y903

Chemical Name and Type of Pesticide: fenoxaprop-ethyl(proposed common name), ethyl 2-[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy] propanoate, 12.5% ai, herbicide.

Trade Name: Whip 1 EC Herbicide
HOE-33171

Chemical Structure:



Physical and Chemical Properties:

See attached information.

American Hoechst is applying for experimental use permit (EUP) to use Whip 1 EC Herbicide for selective postemergence annual and perennial grass control in soybeans. The program will involve 50 tests to treat 30 acres each in 8 regional areas covering 29 states. Treatment of 1500 acres will require 269.25 lbs ai. The proposed program is attached.

2.0 DIRECTIONS FOR USE

See attached label.

3.0 DISCUSSION OF DATA

3.1 HYDROLYSIS

3.1.1 Hydrolysis of HOE 33171, Document No. A24235, translation of document No. A 21394, 13 Jan 1981, Tab # D-34, Vol. 15 of 20, Acc. No. 071800.

Experimental Procedure

Hydrolysis was tested in 0.05 M buffer systems at five pH values:

pH 1,2	KCl + HCl buffer
pH 5	K-biphthalate + NaOH
pH 7	KH_2PO_4 + NaOH
pH 9	H_3BO_3 + KCl +NaOH

Glassware was sterilized by heating in a drying oven for 0.5 hour at 150°C. Buffers were sterilized by boiling for 20 minutes, cooling for one hour, and boiling for another 5 minutes. The

initial test concentration of HOE 33171 was 0.45 ppm. Buffer solutions were incubated in a constant temperature water bath at 36°C for pH1,2; 50°C for pH 5; 40 and 50°C for pH 7, and 20°C for pH 9. Sampling was for varying periods up to 8 days. Analysis was by HPLC, using methylene chloride extractions.

Results

Tables 1-3 summarize the data for buffer solutions at pH 5, 7, and 9. The compound designated HOE 53022 is the free acid hydrolysis product - the only one detected. Extrapolation of the data to 20°C by use of an Arrhenius' equation gave half-life times of 700 days for pH 5 solution, 100 days at pH 7, and 2.4 days at pH 9.

Conclusions

HOE 33171 is expected to be stable to hydrolysis at 20°C in pH 5 and pH 7 solutions, but rapidly hydrolyzed in pH 9 buffer. Under high-temperature test conditions, the free acid (HOE 53022) was the only hydrolysis product. The study satisfies this data requirement.

3.2 AEROBIC SOIL METABOLISM

3.2.1 Aerobic soil metabolism study of the herbicide Hoe 33171-^{14}C, document # A 24450, 23 July 1982, tab # D-37, Acc. No. 071800.

Experimental Procedure

The test compound was uniformly radiolabeled in the chlorophenyl ring of Hoe 33171. Three soils were studied:

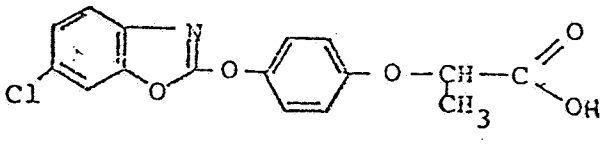
Soils	organic carbon	particles <20 um	pH
a) Loamy sand (Neuhofen neu) (Germany)	2.6%	10.1%	6.8
b) Sandy loam (Hatzenbuhl) (Germany)	1.0%	19.5%	5.2
c) Sandy loam (Agrisearch) (U.S.A)	2.4%	29.0%	6.4

Sieved, moistened (40% capacity) soil was mixed with 3.5 ppm of the labeled herbicide in an Erlenmeyer flask stoppered with cotton wool plugs and incubated in the dark at 22 ± 2°C. Sampling was done at 0, 1, 2, 4, 8, 16, and 32 days by covering the soil of a flask with a acetonitrile/water (80:20) solution and rinsing into a column (Fig. 1). The column was eluted with 400 ml of the solution. Eluate was analyzed by LSC, concentrated, and applied to precoated TLC plates. The evaluation of $^{14}CO_2$ was detected in a closed aeration system (Fig. 2) that tested 1.8 ppm of the herbicide in the soils. The apparatus was aerated daily for two hours. The ethanalamine/methanol column was designed to collect the CO_2. Samples were taken at day 7, 14, 21, 28, 35, and 42.

Results

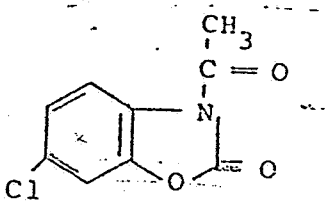
Table 4 summarizes the data from the metabolism of Hoe 33171 and gives a material balance of the radioactivity. The percent of applied ^{14}C decreased to 13.9% for soil a, to 37.1% for soil b, and to 10.9% for soil c by the last sample (day 32). Residues bound to soil increased at each sampling, with a range for the soils of 43.1 to 64.6% on day 32. Three metabolites were detected and identified:

MI: 2-[4-(6-chloro-2-benzoxazolyloxy)-phenoxy]-propionic acid



mol.w. 347

M2: 6-chloro-2,3-dihydro-benzoxazol-2-one



M3: 4-(6-chloro-2-benzoxazolyloxy)-phenol

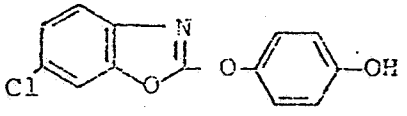


Table 5 gives the amount of $^{14}CO_2$ and volatile metabolites evolved from the soils in 42 days. Figures 3-5 shows the decline curves for Hoe 33171 in the three soils, all of which gave half-lives of less than one day. Since M1 (the free acid of Hoe 33171) is the major metabolite, an estimate of the half-life in each soil was determined by linear regression using the sum of M1 and parent at each sampling period. Figures 6-8 shows the semi-log plots. The t 1/2 ranged from 5-14 days for the three soils.

Conclusion

Hoe 33171 was observed to degrade very rapidly in an aerobic metabolism study using three different soils.

The study is not satisfactory. Additional information is required and questions to be addressed (see recommendation).

3.3 ANAEROBIC SOIL METABOLISM

3.1 Anaerobic soil metabolism study of the herbicide Hoe 33171, document No. A24414, 1 Oct. 1982, tab #D-38, Acc. No. 071800.

Experimental Procedure

The study used the same radiocarbon labeled compound tested in the aerobic soil study, as well as the two soils from Speyer, W. Germany: loamy sand (Neuhofen neu) and sandy loam (Hatzenbuhl). Sieved, moistened soils (40% capacity) were incubated four weeks in the dark at 22 $\pm$ 2°C before being flooded with a peptone solution to obtain anaerobic conditions. Measurement of the redox-potential was used to determine this condition (several days at, or less than, 140 mV). The active ingredient was added, mixed with soil, and the flasks incubated in the dark at 22°C. Sampling was done on day 0, 1, 2, 4, 8, 16, and 32, when the slurry was rinsed onto a column (as with aerobic study) and extracted with acetonitrile/water. Analysis was by LSC and TLC.

Results

Table 6 summarizes the data. Findings were as follows:

1. Very rapid degradation to the free acid (M1 metabolite) and the two other degradates (M2, M3) occurred during day one.

2. M3 degradate not detected beyond day two.

3. Half-life of Hoe 33171 was less than one day.

4. Bound residues increased to 35.0-42.3% by day 32.

5. Calculated half-lives of free acid (M1) were 28 and 29 days in loamy sand and sandy loam, respectively.

Figures 9 and 10 show the decline curves for Hoe 33171 in the test soils. Figures 11 and 12 show the semi-log plot for the degradation of M1, the major metabolite.

Conclusion

While Hoe 33171 appears to degrade very rapidly under anaerobic conditions, the study is unacceptable for several reasons and raises some questions (see Recommendation).

3.4 LEACHING

3.4.1 Leaching study of the herbicide Hoe 033171-^{14}C, document #A24588, 24 Nov. 1982, tab # D-39, Acc. # 071800.

Experimental Procedure

The test compound was uniformly radiolabeled in the chlorophenyl ring moiety. Three soils were used and came from Hoechst's farm station in Arcola, MS. Their characteristics are below:

Soils	organic matter	sand	silt	clay	ph
Silt Loam 1	0.8%	25.2%	62.4%	12.4%	6.5
Silt Loam 2	1.6%	7.2%	70.4%	22.4%	6.4
Silty clay 3	2.0%	1.2%	48.4%	50.4%	6.7

Soil TLC was the method used to determine the leaching potential. Along with Hoe 033171, two reference chemicals, pyrazon and 2,4-D, were chromatographed. After drying, the plates were divided into three columns (one/herbicide) that were divided into 10 sections, excluding the origin. Each section was scraped off the plate, extracted with acetonitrile/water, evaporated, and analyzed by LSC.

Results

Table 7 shows the relationship between sections and Rf-values and Table 8 between mobility class/Rf values. Figures 13-15 are histograms of the distillation of Hoe 033171 on the four replicate plates for each soil. Movement of the maximum amount of radioactivity gave Rf-values of 0.09, 0.07, and 0.06 in soil 1, 2, and 3, respectively (mobility class 1 in all soils). The furthest detectable radioactivity was in sections that gave mobility classes of 3, 3, and 2 in soil 1, 2, and 3, respectively. For reference compound Pyrazon, mobility class 2 was the category for all soils, 2,4-D was in class 4 in soil 1 and class 3 in soils 2 and 3.

Conclusion

Hoe 033171 in soil TLC was found to range from immobile to intermediate mobility with respect to its capacity to leach in the soil types tested.

3.4.2 Leaching study of the herbicide Hoe 033171-^{14}C and its degradates, document # A24716, 22 Dec. 1982, tab D-40, Acc. # 071800.

Experimental Procedure

The procedure followed was very similar to the leaching study just reviewed (section 3.4.1), with the following exceptions:

1. The same three soils were used, but they were not aged. Another soil, a sandy loam (#4) was used for the aging step to provide degrades. Its features are: 2.4% O.M., 30.0% sand, 41.0% silt, 29.0% clay, and pH 6.4

2. Sieved soil was moistened to 40% capacity and incubated two weeks at 22 ± 2°C.

3. The soil was treated with Hoe 033171, incubated 16 days, extracted with acetonitrile/water, and spotted on soil TLC plates.

Results

Tables 9 and 10 are similar to Table 7 and 8 of the first leaching study. Figure 16 gives the Rf-values for the degradates M1, M2, and M3. The mid-point (maximum radioactivity) and furthest Rf value, respectively for the degradates were: M1, 0.17, 0.2; M2, 0.4, 0.45; and M3, 0.53, 0.55. These Rf values correspond to mobility classes of low mobility (class 2) for M1 and intermediate mobility (class 3) for M2 and M3.

Conclusion

The degradates of Hoe 033171, designated M1, M2, and M3, were shown to have low to intermediate mobility in soil TLC using sandy loam soil. This study and the previous one (section 3.4.1) satisfy this data requirement.

4.0 EXECUTIVE SUMMARY

Hoe 33171 was shown to be stable to hydrolysis at 20°C and pH 5, 7, and 9. Aerobic soil metabolism studies indicated half-lives for the parent of <1 day and 5-14 days for major metabolite. An anerobic study gave the same half-life for the parent and 28, 29 days for major degradate. Leaching studies of aged and unaged soils indicate low to intermediate mobility for parent and degradates.

S. Hong 4/30/85
No! It hydrolyzes at pH 9 with a t1/2 = 2.4 days

Leaching: No sandy soil was tested, all soils were pH 6.4-6.7
A silt loam with OM 0.8% was tested.

5.0 RECOMMENDATIONS

5.1 EAB does not concur with the proposed use under the EUP for the following reasons:

1. Of the studies required for an EUP (hydrolysis, aerobic soil metabolism, rotational crop, and fish accumulation), only the hydrolysis requirement is satisfied.

2. For the aerobic soil metabolism study, the following must be addressed:

   (a) It was noted that only the chlorophenyl part of the Hoe 33171 molecule was radiolabeled. Since the M_2 degradate resulted from a splitting off of the phenyl ethyl propionate moiety, it would have been useful to have had the phenyl ring labeled so its fate would be known. One of two options is available:

      (i) The study could be repeated with labeling in the phenyl ring of the phenol ethyl propionate moiety.

      (ii) The fate of this moiety could be discussed and supported from other chemical or environmental studies.

   (b) How do you account for the metabolites M1, M2, and M3 being present at zero time?

   (c) What exactly is meant by zero time sampling?

   (d) The half-life of Hoe 33171 (less than 1 day) and its conversion to the free acid is very rapid. Had these soils been treated in the past with an ester?

3. While the anaerobic study is not an EUP requirement, it is needed for registration and certain concerns we have with it have to be addressed:

   (a) Foreign soils used in lab studies must have the same characteristics as U.S. soils for proposed use. Features to be matched are:

      - soil class
      - % organic matter
      - pH soil
      - ratio of soil bacteria to soil fungi to soil actinomycetes

   (b) EPA environmental chemistry guidelines require aerobic aging of <u>treated</u> soil. The study submitted aged <u>untreated</u> soil.

   (c) How do you account for the high levels of metabolites at zero time sampling?

(d) Soil contains far fewer microbes capable of growing under anaerobic conditions than aerobic conditions, a fact strongly supported by environmental studies. In this study, the half-life of the parent compound was about equal to the value under aerobic conditions, a most unlikely observation. The half-life for the major degradate was several times that under aerobic conditions, an expected and resonable finding. How do you account for the half-life of the parent being the same under aerobic and anaerobic conditions?

4. While the leaching studies are not an EUP requirement, it is needed for registration and was, therefore, reviewed at this time.

5. A rotational crop study, or 18-month restriction placed on label, and fish accumulation (bluegill sunfish, flow-through) study are required for the EUP.

6. Additional comments:

   (a) Residue of concern appears to be the free acid residue under environmental conditions.

   (b) Soil metabolism indicates rapid degradation to the free acid.

   (c) The major degradate is the free acid, which is stable to hydrolysis.

7. Please submit the actual calculations that used Arrhenius equations.

Herbert L. Manning

Herbert L. Manning, Ph.D.
Review Section #1
EAB/HED

Fenoxaprop-ethyl scientific reviews

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