FILE

113601

Date Out EFB: 18 AUG 1983

TO: Wm. Miller
Product Manager 16
TS-767

FROM Dr. Richard Moraski
Acting Chief
Review Section No. 1
Exposure Assessment Branch
Hazard Evaluation Division

Attached please find the environmental fate review of:

Reg./File No.: 11273-22

Chemical: Propetamphos

Type Product Insecticide

Product Name: Safrotin

Company Name: Sandoz

Submission Purpose: Review submitted hydrolysis study

ZBB Code: ? ACTION CODE: 311

Date in: 7/15/83 EFB # 3457

Date Completed: 8/17/83 TAIS (level II) Days

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Deferrals To:

_____ Ecological Effects Branch

_____ Residue Chemistry Branch

_____ Toxicology Branch

1.0 INTRODUCTION

Sandoz, Inc. has submitted an additional hydrolysis study to support their application for registration of Safrotin (Propetamphos, as a i.) as an outdoor perimeter spray for control of cockroaches and other pests.

The application for registration was reviewed in EAB review dated December 21, 1982.

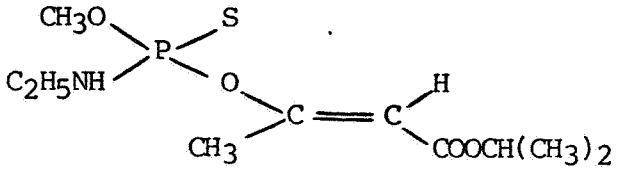
Safrotin is currently registered as an interior applied insecticide.

1.1 Chemical

Common name: Propetamphos

Chemical name: [(E)-1-methylethyl 3-[[(ethylamino)methoxyphosphinothioyl]oxy]-2-butenoate] or (E)-O-2-isopropoxycarbonyl-1-methylvinyl O-methyl ethylphosphoramidothioate

Chemical structure:



2.0 DIRECTIONS FOR USE

No label was included in current submission. EAB assumes that the directions for use reviewed previously are still current.

3.0 DISUCSSION OF DATA

3.1 Sandoz previously submitted a hydrolysis study wherein EAB concluded that the study was not acceptable. The following deficiencies were noted:

- There was no indication as to how the buffers were made, or the pH adjusted.

- There was no indication that glassware was sterilized or that water was bacteria free.

- There was no indication that the hydrolysis was conducted in the dark.

- No material balance was reported.

- The report stated that the P=O metabolite could not be detected, "although being stable during work-up and GLC analysis." No verification of this statement was given.

- No parent or metabolite structures were given.

EAB requested that (1) an additional hydrolysis study be submitted and (2) the registrant agree to conduct an aerobic soil metabolism study and submit the results for review within 18 months.

3.2. Sandoz reply: In response to previous objection, the experiment was conducted using deionized or distilled water and glassware which had been washed, dried at 130 C and stored at rooom temperature. No special sterilization was done as the 1978 Guidelines did not call for it. The protocol suggested in the 1978 Guidelines, viz. H. M. Gomaa et al., Res. Rev. 29, 171-186, also did not mention sterilized glassware or water.

EAB respnse: This is not a valid argument for not using sterilized water and glassware. The 1978 Guidelines listed the the reference, "Krezeminski, S. F. et al. 1975. Fate of Microbial 3-isothiazolone Compounds in the Environment: Modes and rates of Dissipation. J. Ag. Food Chem. 23: 1060-1068" as the primary reference for a procedure for conducting the hydrolysis study. This reference describes the use of deionized sterile water in the hydrolysis study. The Gomaa reference was included in the Guidelines as containing supplemental information on theory and development of rate constants.

It should be pointed out that good laboratory practice dictates that any potential effects from microbial (and also photolytic) activity be eliminated during the hydrolysis study.

3.3. Sandoz reply: Enclosed is a second propetamphos hydrolysis study conducted according to the 1978 EPA Guidelines.

Propetamphos Hydrostability in Aqueous Buffer Solutions of pH 3, 6, 7, and 9 at 25° C and 45° C. Anon. March 29, 1979, Sandoz Report No. 3655/79. EPA Acc. No. 250621.

Procedure:

Aqueous solutions of Titrisol buffer (Merck Co.) and deionized water of pH 3, 6, 7, and 9 were fortified at 5 and 50 ppm with propetamphos (92 + 1% cis-/0.3% trans-isomer) and stored in the dark at 25 ± 0.2° C and 45 ± 1° C.

Samples were taken at 10 minutes, and 4, 7, 14, 21, 28 and 35 (25 C only) days.

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Chloroform was used to extract cis- and trans-propetamphos and the P=O metabolite. The hydrolysis product, isopropyl acetoacetate, was extracted with methylene chloride. Analysis was by GLC using a flame ionization detector and TLC. See Figure 1 for structures.

Recovery was reported to be >90% for all compounds analyzed.

Results

The registrant reported that propetamphos hydrolyzed under all conditions tested (See Tables 1-4). Hydrolysis followed first-order kinetics; the half-life periods were calculated to be:

pH	Half-life (days)	
	25°	45°
3	11	2.4
6	365	82
7	-	17
9	41	3.8

Both the trans-isomer and the P=O metabolite accounted for less than 1% of the degradation product(s) of propetamphos hydrolysis.

The registrant reports that, under normal extraction and analysis no other degradation products were detected by GLC or TLC. However, under certain conditions (acidic and neutral solutions, low temperature, normal extraction and careful evaporation) isopropyl acetoacetate was found as a degradation product. The registrant assumed it rapidly degrades to smaller products (isopropanol, acetone, acetic acid and isopropyl acetate). See Table 7.

Conclusions

EAB notes that:

- Deionized distilled (but not sterilized) water was used in the study.
- The concentration of the buffer solutions or how the solutions were made up is not reported. The HYDR data sheet referenced in the supplemental report, AGRO DOK 1133/73, was not included in the submission.
- The registrant reports that propetamphos hydrolyzed in acidic and alkaline solutions. However, a material balance, including degradation products, was not reported.
- The registrant states that, by an analytical method other than the "normal extraction method" reported, the degradate, isopropyl aceto-acetate, was found. A rationale was not given as to why this method determining this degradate was not routinely used for all analyses.

- The registrant reports in Table 7 that isopropyl acetoacetate accounted for <7% to 20% of the applied material in the buffer solutions after 7 days incubation and maintained at 35° C. It is not known if the 35° C is a type error (for 25° C). or are these the results of an separate, but unreported study? Were additional analyses done for the other sampling periods.

  While this study is lacking in experimental details, EAB can conditionally conclude that propetamphos will be stable in the aqueous environment at environmental temperature and pH. The use of deionized distilled water (but not sterilized) water will not affect this conclusion.

3.4 Sandoz reply: Sandoz agrees to submit the results of an aerobic soil metabolism study within 28 months of the acceptance of this amendment.

EAB response: EAB notes this agreement and awaits the soil metabolism study.

4.0 EXECUTIVE SUMMARY

4.1 Even though the submitted hydrolysis study has many of the deficiencies of the originally submitted hydrolysis study, EAB can conditionally accept the study provided the registrant submits the following additional information:

- How were the buffer solutions made up and what was the final concentration of the solutions? The HYDR data sheet mentioned in the supplemental report, Sandoz No. AGRO DOK 1133/73, was not included in the submsiion.

- Were the samples maintained in the dark? The supplemental report, Sandoz No. AGRO DOK 1133/73, referenced in the study gives general guidelines for this. However, no mention of this fact is made in the study itself.

- Clarification is needed as to why the analytical procedure which qualitatively and quantitatively measured the concentration of the degradation product, isopropyl acetoacetate was not used routinely throughout the study. The data then would represent the material balance.

4.2 The registrant should be informed that the environmental fate studies should follow the current EPA Guideline proctocols and procedures.

Clinton Fletcher
Review Section No. 1
Exposure Assessment Branch
Hazard Evaluation Division

Propetamphos exposure assessment review

Page _____ is not included in this copy.

Pages 7 through 12 are not included in this copy.

The material not included contains the following type of information:

___ Identity of product inert ingredients

___ Identity of product impurities

___ Description of the product manufacturing process

___ Description of product quality control procedures

___ Identity of the source of product ingredients

___ Sales or other commercial/financial information

___ A draft product label

___ The product confidential statement of formula

___ Information about a pending registration action

_X_ FIFRA registration data

___ The document is a duplicate of page(s) _____

___ The document is not responsive to the request

The information not included is generally considered confidential by product registrants. If you have any questions, please contact the individual who prepared the response to your request.