11/19/87

K. Hamernik
✓ D. McLane
P. Datta

Reviewers,

Please look over your part of the attached SIS cover memo for ethoprop to make sure I didn't screw anything up. If I don't hear ~~from~~ you by COB Monday Nov 23rd, I will assume you have no derogatory comments. I am in 812 B (The room with the "Storage" sign on the door.)

Thank you,

R. Perfetti

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

DRAFT

MEMORANDUM

SUBJECT: HED Cover Memorandum for the Ethoprop (FRSTR) Registration Standard

FROM: Amy S. Rispin, Ph.D., Chief
Science Integration Staff
Hazard Evaluation Division (TS-769C)

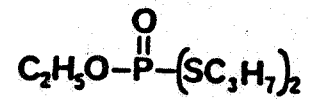
TO: William H. Miller, PM 16
Insecticide-Rodenticide Branch
Registration Division (TS-767C)

Introduction

Ethoprop (O-ethyl S,S-dipropyl phosphorodithioate) is the ANSI approved common name for an insecticide and nemotocide registered in the U.S. by Rhone-Poulenc, Inc. Ethoprop may be applied to a variety of food crops (bananas, beans, cabbage, corn, cucumbers, mushrooms, okra, peanuts, pineapples, potatoes, soybeans, sugarcane, and sweet potatoes) as well as employed for terrestrial nonfood uses for tobacco, turfgrass, ornamental plants, and root dip treatments for citrus seedlings. Ethoprop EC formulations containing 40% or greater ai are Restricted Use pesticides.

The data base for ethoprop contains data gaps in product and residue chemistry, toxicology, ecological effects, and environmental fate. Initial data on mobility in soil requires the submission of ground water information.

The structure for ethoprop is:



There is only one technical ethoprop product which is registered by Rhone-Poulenc, Inc. (EPA Registration No. 359-694). Although product chemistry data may have been submitted in the past, the Agency has determined that these data must be resubmitted for each pesticide because new requirements have been introduced and previously submitted data must be updated.

Residue Chemistry

1. Metabolism

The metabolism of ethoprop in plants is not adequately understood. Additional ^{14}C-radiolabeled experiments on corn, potatoes, and cabbage are needed. No metabolism studies on ruminants and poultry are available, such information is required in order to determine the pathway for metabolism of ethoprop in animals. Tolerances for ethoprop are currently expressed in terms of parent compound per se. At such time as the additional required studies are submitted and reviewed the tolerance definition will be reassessed.

2. Analytical Enforcement Methods

Ethoprop is completely recovered by PAM Vol. 1 protocols II and III and partially recovered by protocol I. No data are available for protocol IV. This data is required. Depending on the outcome of the required metabolism studies additional validated methodology may be needed.

3. Storage Stability

Storage stability studies for appropriate raw agricultural commodities using weathered and fortified samples are needed. Samples histories for previously submitted residue trials are also required.

4. Residues in Raw Agricultural and Processed Commodities and Meat, Milk, Poultry and Eggs

The available data support the tolerances for potatoes, sweet potatoes, bananas, peanut nutmeats, and sugarcane.

The available data are insufficient to assess the tolerances for residues in or on cabbage, lima beans, lima bean forage, snap beans, snap bean forage, soybeans, soybean forage, soybean hay, cucumbers, corn grain, sweet corn K+CWHR, corn forage, and pineapples. Additional field residue data are required for these crops.

No food or feed additive tolerances have been established for residues of ethoprop in any processed commodities of crops having established residue tolerances. Processing studies are needed to determine the need for such food or feed additive tolerances for potatoes, soybeans, corn, peanuts, pineapples, and sugarcane.

Tolerance proposals as well as appropriate supporting residue data are needed for the following raw agricultural commodities of crops having registered uses: bean hay (including snap bean and lima bean hay), soybean straw, peanut hulls, and peanut vines.

Toxicology

1. Acute Effects and Irritation Studies

Available studies indicate that ethoprop is highly toxic to mammals when administered orally, dermally, or via inhalation. Ethoprop is acutely lethal if absorbed through the eye. Additional dermal irritation and dermal sensitation studies are not required at this time. No acute neurotoxicity was observed in the hen.

2. Subchronic Effects

Sufficient data are available to determine subchronic oral toxicity in a nonrodent. The available rat subchronic feeding study is considered supplemental. However, an additional study is not required provided an acceptable rat chronic feeding study is performed.

The 21-day subchronic dermal study showed no treatment related toxicity or mortality. This experiment however

is not considered to be acceptable and therefore, an additional study is required. No additional subchronic studies (90-day dermal, inhalation, or neurotoxicity) are required.

3. Chronic Effects

No acceptable studies for nonrodent and rodent chronic toxicity, oncogenicity (two species), teratogenicity (two species) or reproduction are available. Such data are needed. The 1-year dog chronic feeding study, while not acceptable, need not be repeated because a special study required below will resolve deficiencies in this experiment. Two oncogenicity studies, one in rats and one in mice ,exist for ethoprop and a request for submission of this data has been made. A teratology study in rats submitted previously is considered supplemental.

4. Mutagenic Tests

An acceptable battery of mutagenicity tests (gene mutation, chromosomal abberation, and DNA damage) are available. However an acceptable bone marrow cytogenetic analysis in rats is needed in order to accomplish in vivo confirmation of in vitro findings in the chromosomal abberation studies submitted.

5. Special Studies

A rat metabolism study is needed. No domestic animal safety or dermal absorption data are indicated.

The following additional special studies are required.

a. A special study in rats which will allow the determination of a definitive NOEL for plasma, erythrocyte, and brain cholinesterase inhibition. A protocol should be submitted prior to commencement of this experiment.

b. A subchronic feeding study in dogs which will alleviate issues of decreases in animal body weight gain and the lack of a NOEL for cholinesterase inhibition in the present 1-year study. This experiment should also allow determination of a more sensitive species for cholinesterase inhibition. A protocol should be submitted prior to initiation of this study.

c. An acceptable rat bone marrow cytogenetic analysis

for in vivo confirmation of in vitro cytogenetic findings observed in the chromosomal abberation experiments.

d. Two mouse studies, one an oral gavage in the B6C3F1 mouse and the other a dietary study in another mouse species, which will allow resolution of the question of whether eye lesions observed in the 78-week mouse oncogenicity study were systemic effects of medication with test material.

Tolerance Assessment

Tolerances have been established at 0.02 ppm for residues of ethoprop per se in or on bananas, beans, cabbage, corn, cucumbers, mushrooms, okra, peanuts, pineapples, potatoes, soybeans, sugarcane, and sweet potatoes. Due to a lack of acceptable metabolism (plants and animals), storage stability and residue studies a conclusive tolerance reassessment cannot be completed at this time. A provisional acceptable daily intake (PADI) of 0.000015 mg/kg/day is being used for tolerance evaluations. This PADI is based on a 90-day rat feeding study in which a NOEL for cholinesterase inhibition was estimated to 0.015 mg/kg/day and a thousandfold safety factor was utilized. This PADI has been confirmed by the Toxicology Branch ADI Committee. Additional studies on a rat and a dog are required so that a definitive NOEL in the most sensitive species can be determined. The Theoretical Maximum Residue Contribution (TMRC) to the human diet was based on published tolerances and for the U.S. population was 0.000073 mg/kg/day which is 489% of the PADI. The TMRC exceeded the PADI in all 22 subgroups with the highest exposures being calculated for children 1 to 6 years of age (0.000162 mg/kg/day, 1083% of the PADI) and children 4 years of age (0.000162 mg/kg/day, 1075% of the PADI). Upon receipt of the required residue chemistry and toxicology data, the ethoprop tolerances (as well as the PADI) will be reevaluated.

Ecological Effects

1. Avian Studies

Ethoprop technical is highly toxic to bird species on acute oral, dietary, and dermal basis. Acceptable acute and subacute dietary toxicity studies are available. Field dissipation studies which will more accurately define acute hazards to bird species

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inhabiting treated areas are required. Avian reproduction studies may be needed if it is found that ethoprop residues remain at significant levels in the field for and extended period of time.

2. Aquatic Studies

Technical ethoprop is very highly toxic to aquatic invertebrates. It is moderately to highly toxic to rainbow trout and highly toxic to bluegills, crustaceans, and marine fish species. Ethoprop is slightly toxic to embryolarvae of oyster species. Further assessment of the hazards involved with aquatic organisms cannot be made until certain environmental fate data are submitted and reviewed. At that time an ~~expected~~ estimated environmental concentration (EEC) will be developed. Further aquatic data requirements will be reserved until the EEC and environmental fate data are available.

3. Precautionary Statements

The following precautionary statements are needed on manufacturing-use and end-use product labels.

Manufacturing-Use Products

This pesticide is toxic to aquatic organisms (fish and invertebrates) and extremely toxic to birds. Do not discharge effluent containing this product into lakes, streams, ponds, estuaries, oceans, or public waters unless this product is specifically identified and addressed in a NPDES permit. Do not discharge effluent containing this product to sewer systems without previously notifying the sewage treatment plant authority. For guidance, contact your State Water Board or Regional Office of the EPA.

Granular End-Use Products (Except Turf)

This pesticide is toxic to aquatic organisms (fish and invertebrates) and extremely toxic to birds. Birds in treated areas may be killed. Do not apply directly to water or wetlands

(swamps, bogs, marshes, and potholes). Drift and runoff may be hazardous to aquatic organisms in neighboring areas. Cover or incorporate granules that are spilled during loading or are visible on soil surface in turn areas. Do not contaminate water by cleaning of equipment or disposal of wastes.

Granular End-Use Products (~~Except~~ Turf only)

This pesticide is toxic to aquatic organisms (fish and invertebrates) and extremely toxic to birds. Collect granules spilled during loading. Birds in treated areas may be killed. Do not apply directly to water or wetlands (swamps, bogs, marshes, and potholes). Runoff may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning of equipment or disposal of wastes.

Nongranular End-Use Products (Except ~~Domestic~~ Turf)

This pesticide is toxic to aquatic organisms (fish and invertebrates) and extremely toxic to birds. ~~Cover or disc spill areas~~. Replace with: Collect granules spilled during loading. Birds in treated areas may be killed. Do not apply directly to water or wetlands (swamps, bogs, marshes, and potholes). ~~Drift~~ and runoff may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning of equipment or disposal of wastes.

Nongranular End-Use Products (~~Domestic~~ Turf Only)

This pesticide is toxic to aquatic organisms (fish and invertebrates) and extremely toxic to birds. Birds in treated areas may be killed. Do not apply directly to water or wetlands (swamps, bogs, marshes, and potholes). Drift and runoff may be hazardous to aquatic organisms in neighboring areas. Do not contaminate water by cleaning of equipment or disposal of wastes.

4. Endangered Species

Sufficient data are available to indicate that current registered uses of ethoprop may affect endangered species. Terrestrial EECs for all use patterns except ornamentals and citrus seedling (confined to pots) exceed one-tenth the LC_{50}. Since insect avian and aquatic species are at hazard as a result of the use of ethoprop on corn and soybeans endangered species labeling for these two crops is required.

Exposure Assessment

1. Environmental Fate

Data requirements for soil metabolism of ethoprop (both aerobic and anaerobic) are fulfilled. Partial data gaps exist for the leaching and absorption/desorption requirements. All other data requirements for the remaining pertinent environmental topics are required.

2. Groundwater

Submission of groundwater data for ethoprop is needed. This pesticide was found to be very mobile in two different soil types. Studies required to assess the potential for groundwater contamination include hydrolysis, photolysis in water and soils, leaching of soil degradates, and field dissipation. Due to the incomplete data base no quantitative estimation of the potential for groundwater contamination can be made.

3. Reentry Protection

Foliar and soil dissipation studies are required for Reentry Protection. Dermal and inhalation exposure studies under this topic are an optional requirement at this time.

cc: A. Barton (HED)
S. Johnson (HED)
J. Heckman (MSS)
K. Hamernik (TB)
P. Datta (EAB)
R. Perfetti (RCB)
D. McLane (EEB)

Acute and stimulated field studies show sufficient hazard to wildlife to require the following two field studies:

1. One study with the emulsifiable concentrate (EC) on turf
2. and, one with the granular (G) product on corn or potatoes

Both these studies were required under the first Registration Standard by June 1986. The EC study ~~was not sb~~ has not been received. The G study did not meet the guideline requirements.