Reg. Std
8-1-86

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

AUG 1 1988

AUG 1988

EXPEDITE

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: Propanil Registration Standard - Response to Data Call-In Notice on Rice Metabolism.
EPA Registration Nos. 707-108 and 707-181.
(No MRID Number) [RCB No. 4053]

FROM: Francis D. Griffith, Jr., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Robert J. Taylor, PM 25
Fungicide-Herbicide Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

The review of the metabolism study protocol is being expedited at the request of Edwin F. Tinsworth, Director of the Registration Division (RD) in his memorandum dated July 13, 1988, to Anne L. Barton, Acting Director of Hazard Evaluation Division.

SUMMARY OF RESIDUE CHEMISTRY DEFICIENCIES REMAINING TO BE RESOLVED

Nature of the Residue - Plants

Conduct a propanil in rice and wheat metabolism study.

Background

NPC, Incorporated, on behalf of the Propanil Task Force has submitted by letter dated June 22, 1988, a request for an expedited review of a protocol for propanil, trade named Stam^{R}, for a metabolism study in rice grain, rice straw, and rice processed commodities. The Propanil Task Force request to review a propanil rice metabolism study protocol is a follow-up to the Registration Standard's request for additional propanil plant metabolism data.

The Residue Chemistry Chapter of the Propanil Registration Standard was completed on August 26, 1987. The conclusions on the nature of propanil residue in plants are as follows:

- The available data do not adequately describe the metabolism of propanil in plants because (i) no more than 26 percent of the total ^{14}C-residues in rice grain or straw following foliar or soil treatment with [^{14}C-ring]propanil was identified; (ii) although caustic hydrolysis of bound residues ($\geq$ 50% of total ^{14}C-residues) released significant amounts of 3,4-dichloroaniline (DCA), no ^{14}C-balance data were provided to indicate what percent of total bound ^{14}C-residues were accounted for by metabolites containing the DCA moiety; (iii) it was determined that bound ^{14}C-residues were <u>not</u> incorporated into natural plant constituents; and (iv) no metabolism studies were conducted on other small grains such as wheat, barley, or oats. The following data are required:

  o Metabolism studies in which rice and wheat are treated foliarly and via the soil (in separate tests) with [^{14}C-ring]propanil at a rate sufficiently high to permit complete characterization of ^{14}C-residues in straw and mature grain. Plants should be grown under environmental conditions that approximate actual field conditions (i.e., rice should be flooded within 24 hours of treatment). Wheat should be treated at the 4 or 5 leaf stage and rice at the mid-tillering stage. Plants should be harvested at several intervals thereafter (every 2 weeks) and at maturity. At maturity, straw and grain must be analyzed separately. ^{14}C-Balance data must be presented for each sample analyzed. Conjugated or bound ^{14}C-residues <u>must</u> be characterized. Representative samples from these studies must be analyzed using <u>all</u> current and proposed enforcement procedures (including FDA

2

multiresidue methods) to ascertain that the methods are capable of accurately quantifying all residues of toxicological concern.

Our conclusions and recommendations concerning the proposed propanil rice metabolism study follow.

Conclusion for This Protocol

- The registrant does not have to conduct separate ^{14}C-propanil rice plant metabolism studies from a soil application and a foliar application. A combined foliar and soil application reflects a real world situation and use.

- The registrant should increase the ^{14}C-propanil dose for the foliar application up to 2X (12 lb ai/A) if possible, and the soil application rate should be at least 4X (24 lb ai/A) in order to obtain sufficient ^{14}C-propanil residues to characterize and identify at least 90 percent of the ^{14}C-residue in rice straw and in the paddy rice or rough rice.

- The registrant needs to characterize metabolites conjugated as sugars/amino acids, not identify each sugar/amino acid conjugate.

- Any proposed analytical enforcement method should be validated with the ^{14}C-propanil metabolite residues of toxicological concern.

- RCB has no objections to the proposed protocol that are related to the objective, good laboratory practices, quality assurance, test material, sample storage and identification, documentation, shipping reports, statistical method, and data and sample retention. RCB agrees with the proposed test system growth and sampling scheme.

RCB Recommendations

RCB recommends that the registrant be informed of our comments on the proposed protocol. If the registrant agrees to incorporate our conclusions, then he should proceed with the ^{14}C-propanil rice metabolism study.

Petitioner's Response

In a letter dated June 22, 1987, from Roger A. Novak, Technical Director of the Propanil Task Force to Joanne Miller of the PM 25 Team, the Propanil Task Force presented a proposed protocol to conduct a propanil rice metabolism study. The title of the protocol is "Propanil: Nature of the Residue in Rice - In-Life Phase." The Project No. is 88-3500.

RCB Comments

RCB has reviewed the protocol for a propanil rice metabolism study. We agree with the study's objectives to determine the nature of the ^{14}C-residue at various stages of rice development after treatment with exaggerated rates of ^{14}C-propanil. The registrant proposes to plant Tebonnet, a long grain, early to mid-season variety of rice, in up to 100 pots filled with Louisiana soil. Since the rice pots will be flooded and propanil will be applied at mid-tillering (5 to 7 leaf stage) questions relating to dry-drilled seeding or water-seeded rice are not germane to this protocol.

The registrant proposes a simultaneous or combined soil and foliage treatment of the rice each at the 1X (or 6 lb ai/A rate). Upon further consideration, RCB now agrees with the registrant that the real world situation is a simultaneous soil and foliage application of propanil. The registrant is no longer required to conduct a separate plant metabolism study of ^{14}C-propanil treatment to soil and a separate plant metabolism study of ^{14}C-propanil treatment to rice foliage as required in the Registration Standard. The registrant proposes using ring-labeled ^{14}C-propanil at a specific activity of 20.6 mCi/gram formulated as a typical propanil end-use product. The use of a 1X foliage treatment is acceptable, although if this rate can be increased to a 2X foliage application rate (12 lb ai/A), RCB would prefer this as long as there are no overt toxicological manifestations showing in the rice. We found the proposed soil application rate of 6 lb ai/A (1X) to be too low. We suggest that at a minimum, the registrant use a 4X (24 lb ai) propanil to soil application. Even a 4X to soil may be too low to obtain sufficient rice with enough residue to characterize and identify at least 90 percent of the ^{14}C-residue.

The registrant proposes planting in up to 100 pots with sufficient seed so that there can be intermediate harvests of immature rice to determine the extent of ^{14}C-propanil metabolism. At 28 days after planting, the pots will be flooded to a depth of 1 to 2" above soil surface with ^{14}C-propanil treatment at 45 to 60 days. The water will be

lowered, rice foliage and soil will be treated, then within 24 hours the pots will be reflooded. RCB has no objection to this part of the protocol, nor to the proposed growth conditions.

The proposed sampling of the flood waters and the soil in the pots is not germane to RCB's need to understand the nature of the residue in plants. Obtaining control rice "forage" samples prior to ^{14}C-treatment, then obtaining treated samples immediately after application, intermediate immature samples at the 2 to 3 week and 5 to 6 week after application is acceptable. Likewise, we agree that all senescent leaves should be retained to help determine the mass balance. At maturity, the petitioner proposes separating rice straw from the paddy or green rice. The green/paddy rice will be processed into polished rice, rice hulls, and rice bran. RCB defines rice milled products as polished rice, rice bran, and rice hulls. The registrant should be reminded to adequately describe his rice processing and determine how closely this processing approximates commercial processing. The registrant proposes storing all samples immediately after collecting at -20 `C. RCB suggests that the petitioner be able to account for the time and condition of storage of the paddy rice from harvest through processing until each fraction is stored at -20 `C. The registrant is reminded that at least 90 percent characterization and identification of the ^{14}C-propanil in both rice straw and rice grain should be the registrant's goal. RCB agrees with the proposed sampling and storage scheme.

RCB has no objections to the proposed sample identification, documentation, method of shipping the samples, reports, statistical methods, data and sample retention, good laboratory practices, and quality assurance.

Other Considerations

In a telecon with the registrant, Rohm & Haas (F.D. Griffith - T.D. Rogerson on July 18, 1988) the question arose on how extensive an identification of propanil sugar-amino acid conjugates would be required. After careful consideration, RCB agrees that the registrant need not identify each possible sugar amino acid propanil conjugate that would be cleaved to the aglycone N-(3,4-dichlorophenyl) moiety. Characterization to a N-(3,4-dichlorophenyl) sugar would be sufficient with the proposed method detecting the aglycone. RCB encourages the registrant to validate the proposed enforcement procedure with the ^{14}C-material from this study.

TS-769C:RCB:Reviewer(FDG):CM#2:Rm814B:5570826:JOB:53425:I:C.-DISK:KENCO:8/2/88:dd:vo:ek:dd:edited:fdg:8/5/88.

cc: Reviewer(F.D.Griffith,Jr.), Propanil S.F., Propanil Reg. Std. File (Boodee),ISB/PMSD(Eldredge), Circu.(7), R.F.

RDI:Section Head:R.S.Quick:8/4/88:R.D.Schmitt:8/4/88.