PM50/ISB

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

MAR 8 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: EPA Reg # 014504-5. Mancozeb on Papaya. Residue Study Protocol. No MRID #. DEB # 6369.

FROM: Leung Cheng, PhD, Chemist
Special Registration Section II
Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: Francis Suhre, Section Head
Dietary Exposure Branch
Health Effects Division (H7509C)

TO: B. Maranion, Review Manager 66
Special Review Branch
Special Review/Reregistration Division (H7508C)

Dietary Exposure Branch has been requested to review a papaya EBDC residue study protocol. This EBDC residue study is sponsored by the Papaya Administrative Committee, Honolulu, Hawaii and is to be conducted in cooperation with the University of Hawaii and the Rohm & Haas Company.

The protocol is entitled "Ethylene Bisdithiocarbamate Fungicide Residue Trial - Papaya (Hawaii, USA)." The protocol states that EBDC fungicides are used extensively in papaya culture in Hawaii to control several plant and fruit diseases as a result of frequent rainfall and moderate temperature on the islands. The objective of this study is to generate information for a more realistic dietary exposure assessment and to support proposed reinstatement of mancozeb use in papaya culture in Hawaii. Most uses of EBDC fungicides including papayas had been proposed for cancellation in 12/89.

The product to be used in the residue study will be Dithane M-45 which is formulated as a wettable powder and contains 80% of the active ingredient known as mancozeb. The EPA registration number is 707-162.

Treatments to papayas (Carica papayae var. L. "Solo") would be initiated at flowering, ca 6 months prior to harvest. A total of 13 sprays at 14-day spray intervals would be made. The

treatment rate would be 2 lbs ai/A per treatment. Papayas would be harvested at 0, 1, 2, and 4 days after last treatment. A total of 60 samples would be collected.

A third of the treated samples would be packaged in boxes with "blue ice" and immediately shipped to the Agricultural Biochemistry Department of the University of Hawaii by priority freight for frozen storage. This group of samples is denoted as Preharvest Interval Samples.

Another third of the treated fruits (denoted as Washing Samples in the protocol) would undergo washing operation. Fruits would be immersed in 49 deg C hot water for 20 minutes and then cooled in cold water to 27 deg C pulp temperature. Untreated controls would first be processed to minimize possibility of contamination. Fresh wash water would be used and equipment would be cleaned for each treatment sample. The fruits would be maintained at 27 deg C for 12 hours prior to "use of handling procedures outlined in Preharvest Interval Samples."

The last third of the treated papayas (denoted as Market Basket Samples in the study protocol) also would undergo the washing operation as described under Washing Samples. After washing, the fruits would be stored in clean corrugated cartons for 7 days at 10 deg C and then for 5 days at ambient temperature. These "Market Basket" samples would then be stored frozen or analyzed.

Residue analysis would be conducted at the University of Hawaii, Agricultural Biochemistry Department. Levels of both the parent compound mancozeb and ethylenethiourea (ETU) would be measured in the edible flesh and fruit peel using unspecified analytical methods provided and validated by Rohm & Haas.

DEB Comments

1) According to the information received from the Benefits and Use Division in their memorandum of 5/27/88 (E. Pelletier and G. Ballard), the registered use pattern for mancozeb on papayas allows a maximum number of 14 treatments at rates up to 2 lbs ai/A with a 0-day PHI (Mancozeb Special Review, S. Hummel, 7/13/88). The protocol proposes a total of 13 treatments at the 2 lbs ai/A use rate with PHI's of 0, 1, 2, and 4 days. Residue trials should be conducted with the maximum number of treatments allowed at the maximum use rate, or all labels should be changed such that they are supported by residue data.

2) The protocol does not provide information whether papaya samples would be collected from a single field location or several fields located among the various Hawaii islands. The island of Hawaii produces more than 80% of the papaya grown in the State of

Hawaii. DEB recommends that field trials be conducted at several sites on the island of Hawaii.

3) What is "blue ice"?

4) Regarding the washing procedure described in the submitted protocol (under "Washing Samples"), it is unclear as to the fate of the washed papayas. If these papayas were processed for packing and then transported to Continental U.S., the conditions described for washing and other postharvest handling should mimic the commercial processes.

5) The protocol states that validated residue methods would be provided by Rohm & Haas. Nevertheless, method recovery studies must be run concurrently with the residue analyses of papaya field samples at various fortification levels. Raw data such as sample chromatograms, and standard curves, along with sample calculations, should also be submitted.

6) Residues of mancozeb and ETU have been shown to degrade at varying degrees upon storage, even under frozen conditions. We recommend residue analysis be conducted as soon as possible after sample collection or washing/processing. If samples are stored prior to analysis, storage stability data will be needed as well.

Conclusion and Recommendation

We recommend that the residue study sponsor and their collaborators be made aware of our comments.

Attachment: Pesticide Assessment Guidelines
Magnitude of the Residue: Crop Field Trials

cc:Circ, RF, Special Rev F (S. Hummel), Cheng, PMSD/ISB
RDI:SHummel:FSuhre:3/6/90:EZager:3/7/90
H7509C:DEB:CM#2:Rm810:Cheng:2/23/90:1:3/7/90

Attachment to DEB # 6369

NTIS No. PB86 248192
EPA 540/09-86-151

PESTICIDE ASSESSMENT GUIDELINES

SUBDIVISION O

RESIDUE CHEMISTRY

Series 171-4

Magnitude of the Residue: Crop Field Trials

ADDENDUM ON DATA REPORTING

#2

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Subdivision O - Magnitude of the Residue: Crop Field Trials

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PESTICIDE ASSESSMENT GUIDELINES

RESIDUE CHEMISTRY

Magnitude of the Residue: Crop Field Trials[1/]

Subdivision O, Series 171-4

DATA REPORTING

INTRODUCTION

A. Purpose

Crop field trials to provide residue chemistry data on the magnitude of the residue are required by 40 CFR 158.125 to support the registration of any pesticide intended for use on a food or feed crop under the amended Federal Insecticide, Fungicide, and Rodenticide Act.

Residue chemistry data on raw agricultural commodities (r.a.c.) are used by the Agency to estimate the exposure of the general population to pesticide residues in food, and for setting and enforcing tolerances for pesticide residues in or on raw agricultural foods or feeds under provisions of Section 408 of the Federal Food, Drug, and Cosmetic Act. (Note: Processed foods and feeds are regulated under Section 409 of the Act.)

Residue chemistry data are also needed to support the adequacy of one or more methods for the enforcement of the tolerance, and to support practical methods for removing residues that exceed any proposed tolerances.

Subdivision O (Residue Chemistry) of the EPA Pesticide Assessment Guidelines (§§ 171-3 and §§ 171-4) and the Guidelines on Pesticide Residue Trials developed under the auspices of the Codex Committee on Pesticide Residues (FAO Plant Protection Bulletin, 29:1/2, pp. 12-27, 1981) provide information to aid the petitioner/registrant in conducting crop field trials.

1/ Other aspects of the Magnitude of the Residue (see 40 CFR 158.125: processed food/feed; meat/milk/poultry/eggs; dermal uses; fumigation uses; etc.) will be addressed in separate Data Reporting Guideline documents.

B. Objective

Crop field trial studies should answer the following question: What is the maximum level of "total toxic residue" that will likely result in or on the raw food or feed commodity as a result of application of the pesticide formulated product according to the proposed label directions for use?

The term "total toxic residue" is used to describe the sum of the parent pesticide and its degradation products, metabolites (free or bound), and impurities that are considered to be of toxicological significance, and therefore warrant regulation.

Actual residue data on commodities as consumed should be provided in cases where tolerance level residues lead to unreasonable risks.

Crop grouping considerations should also be addressed, and an effort made to achieve harmonization with applicable International Residue Limits (Codex).

This Data Reporting Guideline is designed to aid the petitioner/registrant in generating reports which are compatible with the Agency's review process. While following this Guideline is not mandatory, data submitters are encouraged to submit complete reports which can be efficiently reviewed by the Agency.

RESPONSE TO PUBLIC COMMENTS

The purpose of this section is to acknowledge and address the concerns expressed in the letters of comment received by the Agency in response to the public notice in Federal Register Volume 50, No. 147, p. 31010, July 31, 1985.

This addendum to the Pesticide Assessment Guidelines (Subdivision O) is to be considered an all-encompassing document. EPA recognizes there are sections in the addendum which do not apply in all cases. Therefore, registrants should exercise scientific judgment in deciding which portions are germane to a specific data submission.

This Data Reporting Guideline is not intended to introduce new data requirements or revisions into the Pesticide Assessment Guidelines (Subdivision O); nor is it intended for use by Agency data reviewers as a mere checklist. It is intended to clarify ambiguities in interpretation of those existing Guidelines, and to organize the submission of data to facilitate the review process.

For comments relating to Good Laboratory Practices (GLPs), the Agency has revised its requirement in this document in recognition that there is currently no regulatory GLP Guideline for chemistry data.

GUIDELINE

The petitioner/registrant's report on crop field trials on a raw agricultural commodity should include all information necessary to provide a complete and accurate description of field trial treatments and procedures; sampling (harvesting), handling, shipping, and storage of the r.a.c.; storage stability validation of the test chemical [and metabolite(s) of toxicological concern] in a plant matrix; residue analyses of field samples for the "total toxic residue" (and for individual components of toxicological concern); validation (recovery studies) of the residue analytical methodology; reporting of the data and statistical analyses; and, quality control measures/precautions taken to ensure the fidelity of these operations. The following is the suggested format for the report.

[Note: The Analytical Method(s) and Storage Stability formats are addressed in separate Data Reporting Guideline documents being developed concurrently.]

MASTER COVER PAGE

Title page and additional documentation requirements (i.e., requirements for data submission and procedures for claims of confidentiality of data) if relevant to the study report should precede the content of the study formatted below. These currently proposed requirements are described in 49 FR (188) 37596 (9/26/84).

MASTER TABLE OF CONTENTS

I. MASTER SUMMARY/INTRODUCTION

A. Purpose of studies [include target pest(s)/disease(s)];

B. Results [including explanations for apparently aberrant, atypical values, or outliers; discussion of geographical representation (major growing areas), seasonal variation (summer/winter, wet/dry, etc.), and representativeness of types and varieties of the r.a.c.; and whether the intended use is claimed to be a "minor use" (ref. 40 CFR 158.60; EPA's policy concerning data requirements for minor uses of pesticides includes the following elements: a crop which is planted on a small total amount of acreage or a use which is otherwise limited such that the potential market volume of the product for that use is inherently small, thus resulting in the risk and exposure associated with the proposed use being correspondingly low. For further discussion, see the EPA Policy Statement on the Minor Uses of Pesticides, OPP-36114.)];

C. Field procedures;

D. Analytical procedures/instrumentation;

E. Method recovery validation data;

F. Storage stability;

G. Discussion [including Quality Control measures taken; statistical treatment(s) of data; and information on the level(s) of the "total toxic residue" (including any individual component(s) of the residue of special concern) in or on the r.a.c. (specific plant part(s)) arising from the use of the pesticide formulated product on the test crop under specific use conditions. Results should also be correlated to the storage stability study.]; and

H. Conclusions.

II. MASTER DATA TABLE(S) AND OTHER GRAPHIC PRESENTATION(S)

A. Summary map (USA, include outside USA, if applicable) of crop field study sites (by crop);

B. Summary table(s) of residue results of individual field trials;

C. Graphic representation(s) (e.g., residue decline), figures, flowcharts, etc.;

D. Summary table(s) of recovery data via the analytical methodology;

E. Summary table(s) of storage stability validation data;

III. INFORMATION/RAW DATA ON INDIVIDUAL FIELD TRIALS (specifically, each individual field trial report should include the following information)

A. Test Substance (Pesticide)

1. Identification of the test pesticide active ingredient (a.i.), including chemical name, common name (ANSI, BSI, ISO), and company developmental/experimental name;

2. Identification of the pesticide formulated product(s) used in the field trial, including trade name, type (EC, WP, G, etc.), and amount of active ingredient per gallon, pound, etc., EPA registration number (if available), manufacturer, and check of composition (% a.i.) prior to its field use;

3. Information on other relevant parameters, as pertinent, e.g., tank mate(s), spray additive(s), carrier (encapsulating polymer, etc.), etc.; and

4. Other (any and all additional information the petitioner considers appropriate and relevant to provide a complete and thorough description of the test chemical).

B. Test Commodity (r.a.c.)

1. Identification of the r.a.c., including type/variety and crop group classification [40 CFR 180.34(f), as revised 6/29/83, 48 FR 29855];

2. Identification of specific crop part(s) harvested; used in residue analytical methodology validations; and subjected to residue analysis for a determination of the "total toxic residue";

3. The developmental stage(s), general condition (immature/mature, green/ripe, fresh/dry, etc.), and size(s) of the r.a.c. at time of pesticide application(s) and at harvesting(s); and

4. Other (any and all additional information the petitioner considers appropriate and relevant to provide a complete and thorough description of the r.a.c.).

C. Test Procedures

1. A detailed description of the experimental design and procedures followed in the growing of the r.a.c., application(s) of the pesticide formulated product(s), and harvesting(s) of samples. The information provided, which may be presented on standardized field sheets, should include (in addition to a description of the test substance and test commodity):

   a. Trial identification number;

   b. Cooperator (name and address), test location (county and state - country, if outside U.S.A.), and year;

   c. Field trial lay-out (e.g., size and number of control and experimental plots, number of plants per plot/unit area, number of rows per plot, length of rows and row spacing);

   d. Cultural treatment(s) [farming practice (cultivation, irrigation, etc.) and cropping system];

   e. Soil characteristics (name/designation of the soil type and its physical and chemical properties, including pH and percent organic matter);

   f. Method(s) of application (air or ground) of the pesticide formulated product(s), description of the application equipment, type of application (band/broadcast, soil/foliar/directed, ULV/concentrate/dilute, other), and, calibration of pesticide application equipment, including methods and dates;

   g. Dose rate(s) (amount of active ingredient and formulated product per acre, row, volume, etc.) and spray volume(s) (per acre, etc.);

h. Number and timing of application(s) [total number, during dormancy, preplant, preemergence, prebloom, etc., between-application-interval(s), and treatment-to-sampling interval(s) (aka TSI or PHI)];

i. Other pesticide(s) applied [identity (name and type of formulated product(s), active ingredient(s)), rate(s), date(s), tank-mate or separate, purpose of use];

j. Climatological data (record of temperatures and rainfall during the growing season from the nearest weather station, and wind speed during applications);

k. Dates [planting/sowing/transplanting, as applicable, other significant dates in the growing of the crop (e.g., husk split for tree crops), pesticide application(s), harvest(s)];

l. Harvest procedures [method of harvesting (mechanical/hand, from the plant/ground/flotation, etc.), type equipment used, number/weight of samples collected per replication and number of replications per treatment level, sample coding (cross-referenced to sample history), etc.];

m. Quality control (control measures/precautions followed to ensure the fidelity of the crop field test); and

n. Other [any and all additional information the petitioner considers appropriate and relevant to provide a complete and thorough description of the growing of the r.a.c., application(s) of the pesticide formulated product(s), and harvesting(s) of samples].

2. A detailed description of the handling, pre-shipping storage, and shipping procedures for harvested r.a.c. samples. The information provided, which may be presented on a standardized form, should include (in addition to a description of the test substance and the test commodity):

a. Sample identification (means of labeling/coding);

b. Conditions [temperatures, container type(s)/size(s), sample size(s), etc.] and duration of storage before shipping;

c. Method(s) of packaging for shipment [container type(s)/size(s), sample size(s), ambient/iced, labeling/coding, etc.];

d. Means of transport from the field to the laboratory;

e. Dates (harvest, pre-shipping storage, shipping, and receipt in the laboratory);

f. Quality control (control measures/precautions followed to ensure the fidelity of harvested samples during handling, pre-shipping storage, and shipping operations); and

g. Other (any and all additional information the petitioner considers appropriate and relevant to provide a complete and thorough description of the handling, preshipping storage, and shipping procedures for harvested samples).

3. A detailed description of the conditions and length of storage of harvested r.a.c. samples following their receipt in the laboratory.

Refer to the Data Reporting Guideline for a Storage Stability Study[2/] for guidance on this subject area.

4. A detailed description of the residue analyses used in determining the "total toxic residue" in r.a.c. field trial and storage stability samples. (Note: If the specified information is provided elsewhere within the overall data submission package, it need not be reiterated here. In that case, a reference to the relevant analytical methodology would be sufficient.)

Refer to the Data Reporting Guideline on Analytical Method(s)[2/] for guidance on this subject area.

5. Method recovery validation studies should be run concurrently with the residue analyses of crop field trial samples from each individual field trial in order to provide information on the recovery level(s) of the test compound(s) from the test substrate(s) at various fortification level(s) using the residue analytical methods, and to establish a validated method sensitivity. The following information specific to the method validations, which may be presented on a standardized form, should include:

a. Experimental design [e.g., identity of test substrate(s) (specific plant part(s)) and test compound(s) (parent/specific metabolite(s)), number and magnitude of fortification levels, number of replicate samples per test compound per fortification level, sample coding, control samples, etc.];

b. Fortification procedure [detail the preparation of the test compound(s) and test substrate(s) and the manner in which the test compound(s) was/were introduced to the test substrate(s)];

c. Dates [test sample preparation (maceration/extraction/etc.), test compound(s) preparation (standard solution(s) of known concentration), residue analyses];

2/ Concurrently in preparation.

d. Residue results [raw data, ppm theoretical/found, procedure(s) for calculating percent recoveries, recovery levels (range), sensitivity and limit of detection]; and

e. Other (any and all additional information the petitioner considers appropriate and relevant to provide a complete and thorough description of analytical methodology validation procedures).

D. Organization of Data Tables and Forms

1. Table(s) of residue assay data for specific plant parts analyzed;

2. Table(s) on residue recovery values;

3. Graph(s), as pertinent (e.g., residue decline);

4. Form(s) containing field trial history information;

5. Form(s) containing harvesting, shipping, storage information;

6. Table(s) of weather data.

IV. CERTIFICATION

A signed and dated certification of authenticity by, and identifying information (typed name, title, affiliation, address, telephone number) on, the personnel responsible for the various phases of this report (e.g., Study Director, Field Supervisor, and Laboratory Supervisor).

V. REFERENCES

VI. APPENDIX(ES)

A. Representative chromatograms, spectra, etc. of reagent blanks, solvent blanks, reference standards, controls, field samples, fortified samples, etc. (cross-referenced to individual field trial study reports);

B. Reprints of published and unpublished literature, company reports, letters, analytical methodology, etc. cited (or used) by the petitioner/registrant (unless physically located elsewhere in the overall data report, in which case cross-referencing will suffice);

C. Other (any relevant material not fitting in any of the other sections of this report).