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HAZARD EVALUATION DIVISION

STANDARD EVALUATION PROCEDURE

MAGNITUDE OF THE RESIDUE:

CROP FIELD TRIALS

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16. Abstract (Limit: 200 words)
The Standard Evaluation Procedure (SEP) for the Magnitude of the Residue: Crop Field Trials is a guidance document primarily intended for Agency reviewers and the regulated industry who evaluate data specified in 40 CFR Part 158.145. The SEP is also intended to provide information to the general public indicating how the Agency evaluates these types of studies. As such, it is designed to supplement Subdivision O of the Pesticide Assessment Guidelines: Residue Chemistry.

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STANDARD EVALUATION PROCEDURE

PREAMBLE

This Standard Evaluation Procedure (SEP) is one of a set of guidance documents which explain the procedures used to evaluate environmental and human health effects data submitted to the Office of Pesticide Programs. The SEPs are designed to ensure comprehensive and consistent treatment of major scientific topics in these reviews and to provide interpretive policy guidance where appropriate. The Standard Evaluation Procedures will be used in conjunction with the appropriate Pesticide Assessment Guidelines and other Agency Guidelines. While the documents were developed to explain specifically the principles of scientific evaluation within the Office of Pesticide Programs, they may also be used by other offices in the Agency in the evaluation of studies and scientific data. The Standard Evaluation Procedures will also serve as valuable internal reference documents and will inform the public and regulated community of important considerations in the evaluation of test data for determining chemical hazards. I believe the SEPs will improve both the quality of science within EPA and, in conjunction with the Pesticide Assessment Guidelines, will lead to more effective use of both public and private resources.

John W. Melone

John W. Melone, Director
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MAGNITUDE OF THE RESIDUE: CROP FIELD TRIALS[1,2]

I. INTRODUCTION

A. Purpose of the Standard Evaluation Procedure

This Standard Evaluation Procedure is designed to aid Residue Chemistry Branch data reviewers in their evaluations of crop field trial studies submitted by petitioners/registrants. This particular Standard Evaluation Procedure document addresses crop raw agricultural commodities.[1]

B. Background Information

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.'s) 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.

C. Objective of Crop Field Trials

Crop field trial studies should answer the following question: What is the maximum level of "total toxic residue" that will

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1/ Other aspects of the Magnitude of the Residue [see 40 CFR 158.125: processed food/feed; meat/milk/poultry/eggs; fumigation uses; dermal uses; post-harvest treatment] will be addressed in separate Standard Evaluation Procedure documents (to be developed in FY 85).

2/ This Standard Evaluation Procedure is to be used in conjunction with the Standard Format for Preparation of Tolerance Petition Reviews (now under development) that describes the content and considerations of a Residue Chemistry Branch data review memorandum.

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.

II. INFORMATION TO BE SUPPLIED

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 special concern]; residue analyses of field samples for the "total toxic residue" [and for individual components of special 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.

A guideline of specific information that should be included in the petitioner/registrant's report of crop field trials is provided in the Residue Chemistry Branch Data Submission Guideline on the Magnitude of the Residue: Crop Field Trials,[3] that complements this Standard Evaluation Procedure. Related information on Nature of the Residue: Processed Food/Feed, Analytical Method(s), and Storage Stability are found in the Standard Evaluation Procedures[3] and Data Submission Guidelines[3] on those subject areas.

III. THE DATA EVALUATION PROCESS

A. Prepare a Summary

The initial step in the evaluation process of crop field trials on a raw agricultural commodity is for the reviewer to carefully examine and summarize the information/data supplied by the petitioner/registrant in his submission to the Agency. Statistical treatments of the data should be independently verified and the quality control precautions noted.

3/ Concurrently in preparation, FY 85.

B. Identify Data Gaps

Using the Data Submission Guideline on Magnitude of the Residue: Crop Field Trials as a guide (in conjunction with the related Guidelines on Analytical Method(s) and Storage Stability), the reviewer should then look for data gaps - omissions in the information supplied by the petitioner/registrant in his report. These should be duly noted in the reviewer's report, and a judgment made as to which are considered significant enough to adversely affect the review process. Those so identified should be communicated back to the petitioner/registrant by the Product Manager for corrective action.

C. Assess the Appropriateness and Adequacy of the Data

The data reviewer then considers the appropriateness (vis-à-vis the intended use) and adequacy of the data/information that has been supplied. The aforereferenced Data Submission Guidelines are a useful guide to the various parameters that need to be considered. Appendix 1 of this document discusses specific aspects of those parameters that warrant consideration.

As an adjunct to these, the reviewer should draw upon the technical guidance in the reviewer aids materials that are available to him, such as the Residue Chemistry Guidelines (a.k.a. Subdivision O of the Pesticide Assessment Guidelines). A listing of some suggested source materials is located in Appendix 2 to this document.

Any perceived deficiencies in the data/information supplied should be identified and explained, with a statement as to what steps should be taken to resolve the deficiencies, so that this information can be relayed back to the petitioner/registrant by the Product Manager for appropriate action.

Note: As stated in Footnote 1, other aspects of the Magnitude of the Residue, such as processed food/feed and meat/milk/poultry/eggs considerations are to be addressed in separate Standard Evaluation Procedure documents (to be developed in FY 85). Those considerations are applicable whenever a r.a.c. (or parts thereof) may be utilized as an item of livestock or poultry feed, or may be processed into feed items or human foods.

D. Determine the Need for Deferral/Referral(s) to Other HED Branches

In considering the appropriateness and adequacy of the data/information that have been supplied, the data reviewer must also determine if deferral/referral(s) to other HED Branch(es) are germane to reaching that decision.

If so, the specific nature of the deferral/referral(s) should be clearly and succinctly stated and directed to the specific Branch(es) whose input is sought. In the interim period until the response(s) to such deferral/referral(s) are received, final judgment on the issue(s) in question should be withheld.

E. Conclude if the Requested Action is Supportable

As the last step in the data evaluation process, the data reviewer makes a judgment as to whether the submitted data/information support the requested action (tolerance/registration) of the data submitter.

If the data are not supportive, possible alternative action(s) that may be taken by the petitioner/registrant are suggested.

If deficiencies/omissions exist in the submitted data base, the reviewer may have to defer judgment until such time as appropriate corrective action has been rendered by the petitioner/registrant.

(Note: As stated in D above, if deferral/referral(s) to other HED Branch(es) have been made, final judgment will need to be held in abeyance pending the response to such deferral/referral(s).)

IV. REVIEWER AIDS

There are a large number and variety of source materials that are available to assist the data reviewer in the evaluation process. A listing of some of the more useful references that reside within the Branch is provided in Appendix 2 to this document.

APPENDIX 1

MAJOR POINTS TO CONSIDER IN EVALUATING CROP FIELD TRIAL DATA

Include the following:

A. Field Treatments and Harvesting

1. The R.A.C.

- Has the r.a.c. been adequately identified in all the field trials?
- Are an adequate number of types and varieties represented?
- Are the commercially important varieties represented?
- Is it clear what specific plant part(s) were harvested?
- Have the developmental stage(s) and general condition (e.g., immature/mature, green/ripe, fresh/dry, etc.) of the r.a.c. at time of pesticide application(s) and at harvest been specified?
- Were the r.a.c. samples in any way trimmed, cleaned, or otherwise subjected to a means of residue removal at time of harvest? If so, were the recommended procedures of P.A.M. I, §§141-2 followed?
- Are there livestock or poultry feed items associated with the r.a.c.? If so, are animal metabolism and feeding studies available? (Note: these concerns will be addressed in separate Standard Evaluation Procedures to be developed in FY 85.)
- Is the r.a.c. normally processed into feed or food items? If so, have processing studies been conducted? (Ref. Footnote 1, page 1, this document.)
- Is supplementary information available for the pesticide in other reports by the petitioner/registrant on this r.a.c. or botanically related r.a.c.'s that can be translated to support the data base, if needed?
- Are data for the pesticide under similar use conditions available on the representative r.a.c.'s of the crop group to which this r.a.c. belongs and, if so, should a crop group action be considered?
- Are the typical growing seasons (summer/winter; wet/dry) of the r.a.c. represented, especially by field trial data from CA and/or FL?

- Have geographically representative data been submitted for the major growing areas of the r.a.c. (ref. USDA Agricultural Statistics)?

(Note: Determining factors as to what constitutes "adequate geographic representation" include how widespread the crop is grown, its economic importance and national acreage, the range of conditions under which it is grown, whether a minor crop or minor use is involved, what the intended use pattern is, what data and tolerances exist on botanically related crops treated with the same pesticide via a similar use pattern, and the general concern over the toxicity of the pesticide.)

- Is this r.a.c. considered a "minor crop" (i.e., limited acreage and low exposure)?
- Have there been experimental use permits/temporary tolerances, Section 18 exemptions, or Section 24(c) registrations for the r.a.c. treated with this pesticide? Permanent tolerance petition requests?
- Are there Codex/FAO Monograph data available for this r.a.c. or botanically related r.a.c.'s treated with this pesticide?
- Are there international residue limits (IRL's) established for use of this pesticide on this r.a.c. and, if so, upon what use(s) were they established and what components of the residue are regulated? What would be required for harmonization with any such IRL's?
- Is there any other unpublished or published information known to us re this pesticide and r.a.c. use that must be taken into consideration?
- Are all the important dates relative to the growing and harvesting of the r.a.c. reported?

2. <u>The Pesticide</u>

- Does each field trial specify what pesticide formulated product(s) were applied?
- Has each pesticide formulated product been adequately identified? (Detailed consideration of this should be addressed in evaluating the formulation(s); this will be the subject of a separate Standard Evaluation Procedure to be developed in FY 85.)
- Has the EPA Registration Number been given?
- Has the type of formulation (WP, EC, G, etc.) been specified?
- Has the active ingredient (a.i.) in the formulated product been identified?
- Is the purity of the a.i. known? Are there impurities

of concern?
- Is the percent a.i. in the formulated product stated?
- Is the amount of a.i. per gallon, pound, etc. of formulated product given? Are metric equivalents given?
- Is the photochemical stability of the pesticide formulated product known?
- Are the registered label(s) and proposed supplemental label(s) provided (or available somewhere in the over-all data package; e.g., Section B of a petition)?
- Were the field trials conducted with the proposed commercial pesticide formulation(s) of intended use?
- Were spray adjuvants used with the formulation and, if so, are they identified as to nature and amount? Does the proposed use indicate spray adjuvants are intended to be used?
- Were there any tank-mates or other pesticides applied to the r.a.c. and, if so, have they been adequately identified?
- Was there any special carrier involved in the application of the pesticide (e.g., encapsulating polymer, cigarette filter tips, etc.)?
- Is information available (e.g., Section A of a petition) on the stability and solubility of the formulated product(s)?
- Has this chemical been RPAR'd and, if so, what is the current status?
- Is there a Registration Standard on this chemical and, if so, is it being used in the evaluation of these data?

3. <u>The Experimental Design</u>

- Were field trials carried out in the major areas of cultivation or production of the r.a.c. and sited to cover the range of representative conditions (climatic, seasonal, soil, cropping system, farming practice, etc.) under which it is normally grown?
- Are the field trial lay-outs sufficiently described and of adequate design (i.e., inclusion of control plots, large enough plots, etc.)?
- Are there data for successive crop years?
- Are trials properly identified and the collected samples adequately labeled, dated, and coded?
- Is the method of harvesting (mechanical/hand; from the plant/ground/flotation; etc.) described?
- What steps were taken to assure random and representative sampling?

- Is the intended use considered a "minor use" in terms of exposure?
- Were there a sufficient number of field trials conducted on the r.a.c. to support the requested action of the data submitter?

(Note: This is a judgment call and is influenced by the economic importance of the r.a.c., national acreage of the r.a.c., the range of conditions under which it is grown, how widespread it is grown, how closely the trials corresponded with the intended use pattern(s), whether exaggerated rate and residue decline data are available, whether a minor crop or minor use is involved, the data and established tolerances already available on botanically related crops treated with the pesticide under similar conditions of use, the nature of the requested action of the data submitter, and the general concern over the toxicity of the pesticide.)

4. Application of the Pesticide

- Do the field trials reflect the intended use (proposed labeling) of the pesticide on the r.a.c.?
- Are data available reflecting the maximum proposed use conditions (e.g., maximum dose rate(s), maximum number of applications, minimum application intervals, minimum preharvest interval (PHI), etc.)? If not, are the available data sufficient to allow for extrapolation?
- Do the method(s) of application (air/ground) and the type of application(s) [band/broadcast, soil/foliar/directed, ultralow volume (ULV)/concentrate/dilute, etc.) reflect the intended use?
- Are data available reflecting the minimum spray gallonage per acre, especially for ULV intended uses?
- Are label restrictions needed?
- Are exaggerated rate and residue decline data (varying PHIs) available?
- Was a description of the pesticide application equipment provided?
- Was the application equipment used similar to that in local commercial practice?
- Are dose rates and spray volumes reported in a manner (e.g., lbs a.i./A or, for tree crops, for example, X lbs a.i. per Y gallons, use Z gallons per acre) that is consistent with normal practice and with the directions on the proposed labeling? Are metric equivalents provided?
- Are the dates, number(s) and timing of the application(s) given? Is this information tied in with the developmental stage(s) of the r.a.c.?
- Is information provided on tank-mates or other pesticide(s) applied, if applicable (formulation(s), rate(s), date(s) applied, etc.)?

5. Quality Control

- Are quality control measures to ensure the fidelity of the crop field trials described?
- Were proper records (e.g., field trial/sample history, dates, weather, etc.) kept and duly reported?
- Are responsible personnel adequately identified? Was a petitioner/registrant contact person identified and a telephone number provided?
- Was the application equipment calibrated?

B. Handling, Pre-Shipping Storage, and Shipping Procedures for Harvested R.A.C. Samples

1. The R.A.C.

- Were the r.a.c. samples in any way trimmed, cleaned, or otherwise subjected to a means of residue removal during these operations? If so, were the procedures recommended in P.A.M. I, §§ 141-2 followed?
- How were the r.a.c. samples stored between harvesting and shipping (temperature, humidity, container type(s)/size(s), etc.)?
- How soon after harvesting did the r.a.c. samples enter storage?
- How long between harvesting and shipping?
- Were specific dates given for each of these operations for each of the field trials?
- Was any sample compositing or subsampling done at these stages? If so, were details given?

2. General Procedure

- What were the method(s) of packaging samples for shipment (container type(s)/size(s); sample sizes; ambient/iced; labeling/dating/coding)?
- What was the means of shipping the samples to the laboratory?
- Were the dates of harvesting, entry into storage before shipping, and shipping given?

3. Quality Control

- What quality assurance measures were taken to ensure the fidelity of harvested r.a.c. samples?
- Were adequate records kept and has sufficient information been submitted?
- Were responsible personnel identified? Was a petitioner/registrant contact person identified and a telephone number provided?

C. Conditions and Length of Storage of Harvested R.A.C. Samples (following their receipt in the laboratory and prior to residue analysis)

1. The R.A.C.

- Were the r.a.c. samples in any way trimmed, cleaned, or otherwise subjected to a means of residue removal upon their receipt in the laboratory and prior to entering storage? If so, were the recommended procedures of P.A.M. I, §§ 141-2 followed?
- Were the r.a.c. samples stored whole, chopped, as an extract, etc.?
- Was any sample compositing or subsampling done prior to storage? If so, were details given? Were the same sample code numbers maintained?

2. General Procedure

- What were the conditions of storage (temperature, humidity, container type(s)/size(s), sample weights, etc.)?
- What was the extraction procedure (if applicable)?
- What dates were samples received in the laboratory; subsampled/composited (if applicable); chopped or extracted (if applicable); and entered into storage?

3. Quality Control

- What quality assurance measures were taken to ensure the fidelity of harvested r.a.c. samples?
- Were adequate records kept and has sufficient information been submitted?
- Were responsible personnel identified? Was a petitioner/registrant contact person identified and a telephone number provided?

D. Storage Stability Validation Testing

Refer to the Standard Evaluation Procedure on Storage Stability[4] for guidance on this subject area.

E. Analyses to Determine the "Total Toxic Residue" in Samples From Supervised R.A.C. Field Trials

1. The R.A.C.

- What specific plant part(s) were subjected to residue analysis for a determination of the "total toxic residue?"

4/ Concurrently in preparation, FY 85.

- Were all the appropriate plant part(s) subjected to residue analysis? (Ref. Table II, Residue Chemistry Guidelines.)
- Are there food or feed items associated with the r.a.c.? (If so, refer to the Standard Evaluation Procedure dealing with that topic (to be developed in FY 85).)
- Were the r.a.c. samples in any way trimmed, cleaned, or otherwise subjected to a means of residue removal in preparation for the analysis of the "total toxic residue?" If so, were the recommended procedures of P.A.M. I, §§ 141-2 followed?
- Was any sample compositing or subsampling done in preparation for analysis of the "total toxic residue?" If so, were details given? Were the same sample code numbers maintained?
- Was the sample/laboratory coding sufficiently clear so that the history of the r.a.c. sample(s) could be traced (e.g., treatment regimen, harvest date, length of storage, extraction date, etc.)?
- Were control samples (field blanks, reagent blanks) carried through the analytical procedure?
- Were there replicate r.a.c. samples per field treatment regimen per plant matrix?

2. Residue Methodology and Instrumentation

Refer to the Standard Evaluation Procedure on Analytical Method(s)[5] for guidance on this subject area.

3. Analytical Methodology Residue Results

- Were blank values reasonably low? If not, is an explanation provided?
- Are all the raw data reported rather than just average values?
- Were any correction factors [e.g., method recovery, extraction efficiency, field blanks, storage stability] applied to the residue values reported?
- Is the method of calculating the residue values adequately described [formulae, standard curves, etc.], and illustrated, and the raw data sufficiently detailed so that independent calculations to verify the reported results can be made?
- Were the residue values reasonably uniform for replicate samples?

5/ Concurrently in preparation, FY 85.

- Does the petitioner/registrant claim any of the residue values are outliners and, if so, can this claim be supported?
- How do these residue results compare with those on related botanical r.a.c.'s treated with this same pesticide via the same, or similar, use pattern(s) [provided such data are available]?
- How do these residue results compare with previously submitted data [e.g., EUP/temporary tolerance, Section 18 or 24(c) exemptions] for this r.a.c. treated with this same pesticide via the same, or similar, use pattern(s) [provided such data are available]?
- Do these residue results support the action requested by the data submitter? If not, what action(s) should the data submitter undertake to resolve the perceived deficiencies?
- Are residue decline data [residues (ppm) vs. time (PHI)] provided?
- Can harmonization with international residue limits be achieved [if applicable]? If not, why not?
- Is there a Registration Standard for this pesticide and, if so, is it being used by the reviewer in the evaluation of these data?

4. <u>Quality Control</u>

- What quality assurance measures were taken to ensure the fidelity of the analytical methodology residue analyses?
- Was the sample/laboratory coding sufficiently clear so that the history of the sample(s) used could be traced?
- Were the analyst's worksheets provided? Are they sufficiently detailed?
- Were the person(s) [supervisor, analyst] responsible for the analytical methodology residue analyses identified [name, title, organization, address, and telephone number]?
- Were the analytical methodology residue analyses test report(s) authenticated (signed) by the responsible personnel?
- Is a contact person for the petitioner/registrant given with title, address, and telephone number?
- Were representative chromatograms, spectra, etc., as applicable, provided? Are adequate clean-up and determination [i.e., low background "noise", adequate signal-to-noise ratio, well-defined peaks rather than shoulder bands, etc.] of the test compound(s) indicated? The level of claimed sensitivity valid?

- Was the methodology tested for possible interference(s) from other registered pesticides?
- Are the calibration procedures for the instrumentation described?
- Were tests performed for interference from storage containers, reagents, plant substrates, plastic labware, etc.?
- If statistical analyses were performed and applied to the results of the analytical methodology residue determinations, is sufficient information provided to independently validate the results?
- Is a need for a laboratory audit indicated?

F. Analytical Methodology Validation/Recovery Testing

1. The R.A.C.

- What specific plant part(s) were subjected to analytical methodology validation/recovery testing?
- Were the r.a.c. samples in any way trimmed, cleaned, or otherwise subjected to a means of residue removal in preparation for the analytical methodology validation/recovery testing? If so, were the recommended procedures of P.A.M. I, §§ 141-2 followed?
- Was any sample compositing or subsampling done in preparation for analytical methodology validation/recovery testing? If so, were details given? Were the same sample code numbers maintained?
- In what form [whole, chopped, extract, etc.] were the r.a.c. samples [i.e., plant matrices] when they were fortified?

2. The Test Compound(s)

- Were analytical reference grade standards of the parent pesticide and any metabolite(s) of especial concern [normally those which, in addition to the parent, comprise the "total toxic residue," unless present in very minor amounts] used for fortifications? Was the purity of these standards given?
- Is it clear what test compound(s) were used for fortification? For each of the plant matrices tested?
- Were the fortification ["spiking"] level(s) given for each test compound? For each of the plant matrices tested?

- Is it described how the test compound(s) were prepared for the fortification process [i.e., what solute(s), concentration of the standard solution(s), dilution factors, etc.]?
- If "spiking" with a mixture of test compounds, was testing done to ensure interference would be no problem?

3. The Experimental Design

- Were all the necessary compounds [parent plus metabolite(s) comprising the "total toxic residue"] and plant matrices [specific r.a.c. parts] tested for analytical methodology validation/recovery?
- Were the number and magnitude of the fortification levels adequate and appropriate?
- Was there a fortification level to establish a validated sensitivity level?
- Was there a fortification level near the proposed tolerance level?
- Were control samples [field blanks, reagent blanks] carried through the procedure?
- Were the analytical methodology validation/recovery tests conducted in conjunction with the analyses of residues in r.a.c. samples from each of the supervised crop field trials, or as a separate study?
- Were there replicate samples per test compound per fortification level per plant matrix?
- Are all the significant dates given [date of samples receipt in laboratory; dates and length of storage, if applicable; dates of test sample preparation (chopping, extraction, etc.); date of test compound(s) preparation (standard reference solutions); residue analysis, including the determinative step]?

4. Residue Methodology and Instrumentation

- Was more than one analytical method used in the analysis of r.a.c. field trial samples for the "total toxic residue" [i.e., a "total" residue method and perhaps separate method(s) for the metabolite(s) of concern] and, if so, were each of those methods subjected to validation/recovery testing?
- Was the analytical methodology adequately identified [e.g., title/designation/date and source]?
- Is a complete copy [non-CBI] of each analytical method that was used in the validation/recovery study testing provided [or available in the over-all data package] with a description of the principles and the stepwise procedure [extraction/clean-up, derivatization, determination], and is it clear what chemical species could be determined?

- Is it clear if modifications were made in the analytical procedure(s) and, if so, are they adequately described?
- Is it clear at what step in the analytical procedure(s) the fortification occurred, and how this was accomplished?
- Was the extraction efficiency of the analytical methodology demonstrated [especially if dry r.a.c. substrates were used or if the presence of "bound" residues is suspected]?
- Were method sensitivity and the limit of detection given? Were they suitably low?
- Was an internal standard used?
- Were any difficulties encountered in the procedure [e.g., emulsions, etc.] and, if so, were they adequately described and overcome?
- Were any esoteric reagents/equipment/instrumentation used?
- Are the instrumentation [type, type/specificity of detector(s), column(s) (size, packing materials), carrier gas(es), etc.] and operating parameters [flow rate(s), temperature(s), voltage, etc.] specified? Adequately described?
- How long did it take the analyst to run a sample completely through the analytical procedure, including the determinative step?

5. <u>Analytical Methodology Validation/Recovery Results</u>

- Do the results indicate the recoverability of the test compound(s) in the plant matrices?
- Are recovery values acceptably high [$\geq$ 70%, except in special cases; ref. Residue Chemistry Guidelines]?
- Were blank values reasonably low? If not, is an explanation provided?
- Are all the raw data reported rather than just average values?
- Were any correction factors [e.g., extraction efficiency, field blanks, etc.] applied to the residue values/recovery values reported?
- Are the methods of calculating the residue level and percent recovery adequately described [formulae, standard curves, etc.], and illustrated, and the raw data sufficiently detailed so that independent calculations to verify the reported results can be made?

6. <u>Quality Control</u>

- What quality assurance measures were taken to ensure the fidelity of the analytical methodology validation/recovery testing?

- Was the sample/laboratory coding sufficiently clear so that the history of the sample(s) used could be traced?
- Were the analyst's worksheets provided? Are they sufficiently detailed?
- Were the person(s) [supervisor, analyst] responsible for the analytical methodology validation/recovery testing identified [name, title, organization, address, telephone number]?
- Were the analytical methodology validation/recovery test report(s) authenticated (signed) by the responsible personnel?
- Is a contact person for the petitioner/registrant given with title, address, and telephone number?
- Were representative chromatograms, spectra, etc., as applicable, provided? Are adequate clean-up and determination [i.e., low background "noise", adequate signal-to-noise ratio, well-defined peaks rather than shoulder bands, etc.] of the test compound(s) indicated?
- Were the recovery values reasonably uniform for replicate samples?
- Are the calibration procedures for the instrumentation described?
- Were tests performed for interference from storage containers, reagents, plant substrates, plastic labware, etc.?
- If analytical methodology validation/recovery tests were performed in conjunction with the analyses of residues in r.a.c. samples from each of the supervised crop field trials, were the reference standards solutions freshly prepared each day? If not, was their stability monitored?
- If statistical analyses were performed and applied to the results of the analytical methodology validation/recovery testing, is sufficient information provided to independently validate the results?
- Is a need for a laboratory audit indicated?

APPENDIX 2

REVIEWER AIDS MATERIALS[6]

Following is a listing of some of the more useful source materials within the Residue Chemistry Branch that could prove helpful in reviewing crop field trial studies:

(1) Federal Food, Drug, and Cosmetic Act, as amended, §§ 408-409;

(2) Federal Insecticide, Fungicide, and Rodenticide Act, as amended;

(3) Subdivision O [Residue Chemistry] of the Pesticide Assessment Guidelines, §171-3 and §171-4, prepared by OPTS/EPA, Washington, D.C. (1982);

(4) Subdivision D [Product Chemistry] of the Pesticide Assessment Guidelines, prepared by OPTS/EPA, Washington, D.C. (1982);

(5) Code of Federal Regulations [40 CFR 158 and 180; 21 CFR 193 and 561], General Services Administration, Washington, D.C., updated annually;

(6) Pesticide Chemical News Guide, R. E. Duggan, editor, Food Chemical News, Inc., Washington, D.C., 1982, updated monthly;

(7) "Guidelines on Pesticide Residue Trials to Provide Data for the Registering of Pesticides and the Establishment of Maximum Residue Limits," FAO Plant Protection Bulletin, 29:1/2, pp. 12-27 (1981);

(8) "Guidelines for Data Acquisition and Data Quality Evaluation in Environmental Chemistry", Anal. Chem. 52, 2242-2248 (1980);

(9) Acceptable Common Names and Chemical Names for the Ingredient Statement on Pesticide Labels, 4th ed., C. R. Blalock, et al., editors, OPP/EPA, 1979, available from National Technical Information Service, Springfield, VA;

6/ A comprehensive listing is to be compiled in the future.

(10) Farm Chemicals Handbook, Meister Publishing Co., Willoughby, OH, updated annually;

(11) Nanogen Index: A Dictionary of Pesticides and Chemical Pollutants, K. Packer, editor, Nanogens International, Freedom, CA, 1975 (updated periodically by supplements);

(12) U.S.D.A. Agricultural Statistics, U.S. Government Printing Office, Washington, D.C., updated annually;

(13) Crop Grouping Classification [40 CFR 180.34(f), as revised 6/29/83 (48 FR 29855)];

(14) F.D.A. Pesticide Analytical Manual, Volumes I and II, available from the National Technical Information Service, Springfield VA;

(15) Plants Consumed by Man, B. Brouk, Academic Press, NY (1975);

(16) Principles of Field Crop Production, 3d ed., J. H. Martin, W. H. Leonard, and D. L. Stamp, Macmillan Publishing Co., Inc., NY (1976);

(17) Crop Production, 4th ed., R. J. Delorit, L. J. Greub, and H. L. Ahlgren, Prentice-Hall, Inc., NJ (1974);

(18) Food and Feed Crops of the United States, J. R. Magness, G. M. Markle, and C. C. Compton, Rutgers University, NJ (1971);

(19) McGraw-Hill Encyclopedia of Food, Agriculture & Nutrition, D. N. Lapedes, editor-in-chief, McGraw-Hill Book Company, NY (1977);

(20) "Guide for Estimating Toxic Residues in Animal Feeds or Diets" prepared for the E.P.A. by Lorin E. Harris, available from National Technical Information Service, Springfield, VA;

(21) Feeds and Feeding, Abridged: The Essentials of the Feeding, Care, and Management of Farm Animals, Including Poultry, F. B. Morrison, 9th ed., The Morrison Publishing Co., Ithaca, NY (1958);

(22) Statistical Methods Applied to Experiments in Agriculture and Biology, 7th. ed., G. W. Snedecor, Iowa State College Press, Ames, IA (1980);

(23) Foods and Food Production Encyclopedia, D. M. Considine and G. D. Considine, Van Nostrand Reinhold Company, NY (1982);

(24) Registration Standards on various individual pesticides, prepared by OPTS/EPA, (several issued each fiscal year);

(25) Residue Chemistry Branch files: petition and registration files; cultural practices; reviewer aids; policies; foreign uses; subject files; reading files; card catalogue; et al.;

(26) Various reference texts and journal publications of a scientific or agricultural nature, including FAO/Codex Monographs.