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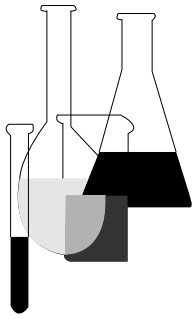
Residue Chemistry Test Guidelines

OPPTS 860.1850 Confined Accumulation in Rotational Crops



“Public Draft”

INTRODUCTION

This guideline is one of a series of test guidelines that have been developed by the Office of Prevention, Pesticides and Toxic Substances, United States Environmental Protection Agency for use in the testing of pesticides and toxic substances, and the development of test data that must be submitted to the Agency for review under Federal regulations.

The Office of Prevention, Pesticides and Toxic Substances (OPPTS) has developed this guideline through a process of harmonization that blended the testing guidance and requirements that existed in the Office of Pollution Prevention and Toxics (OPPT) and appeared in Title 40, Chapter I, Subchapter R of the Code of Federal Regulations (CFR), the Office of Pesticide Programs (OPP) which appeared in publications of the National Technical Information Service (NTIS) and the guidelines published by the Organization for Economic Cooperation and Development (OECD).

The purpose of harmonizing these guidelines into a single set of OPPTS guidelines is to minimize variations among the testing procedures that must be performed to meet the data requirements of the U. S. Environmental Protection Agency under the Toxic Substances Control Act (15 U.S.C. 2601) and the Federal Insecticide, Fungicide and Rodenticide Act (7 U.S.C. 136, *et seq.*).

Public Draft Access Information: This draft guideline is part of a series of related harmonized guidelines that need to be considered as a unit. *For copies:* These guidelines are available electronically from the EPA Public Access Gopher (gopher.epa.gov) under the heading ''Environmental Test Methods and Guidelines'' or in paper by contacting the OPP Public Docket at (703) 305–5805 or by e-mail: guidelines@epamail.epa.gov.

To Submit Comments: Interested persons are invited to submit comments. By mail: Public Docket and Freedom of Information Section, Office of Pesticide Programs, Field Operations Division (7506C), Environmental Protection Agency, 401 M St. SW., Washington, DC 20460. In person: bring to: Rm. 1132, Crystal Mall #2, 1921 Jefferson Davis Highway, Arlington, VA. Comments may also be submitted electronically by sending electronic mail (e-mail) to: guidelines@epamail.epa.gov.

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OPPTS 860.1850 Confined accumulation in rotational crops.

(a) Scope.

(1) Applicability. This guideline is intended to meet testing requirements of both the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) (7 U.S.C. 136, et seq.) and the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301, et seq.)

(2) Background. The source material used in developing this harmonized OPPTS test guideline is the OPP guideline 165-1. This OPPTS guideline should be used in conjunction with OPPTS guideline 860.1000, Background, which provides general information and overall guidance for the 860 series on Residue Chemistry.

(b) Purpose. Data from confined accumulation studies on rotational crops will enable the Agency to determine the nature and amount of pesticide residue uptake in rotational crops. Such data are used to establish realistic crop rotation restrictions (time from application to a time when crops can be rotated) or to provide information for determining if limited field trials are needed for rotational crops.

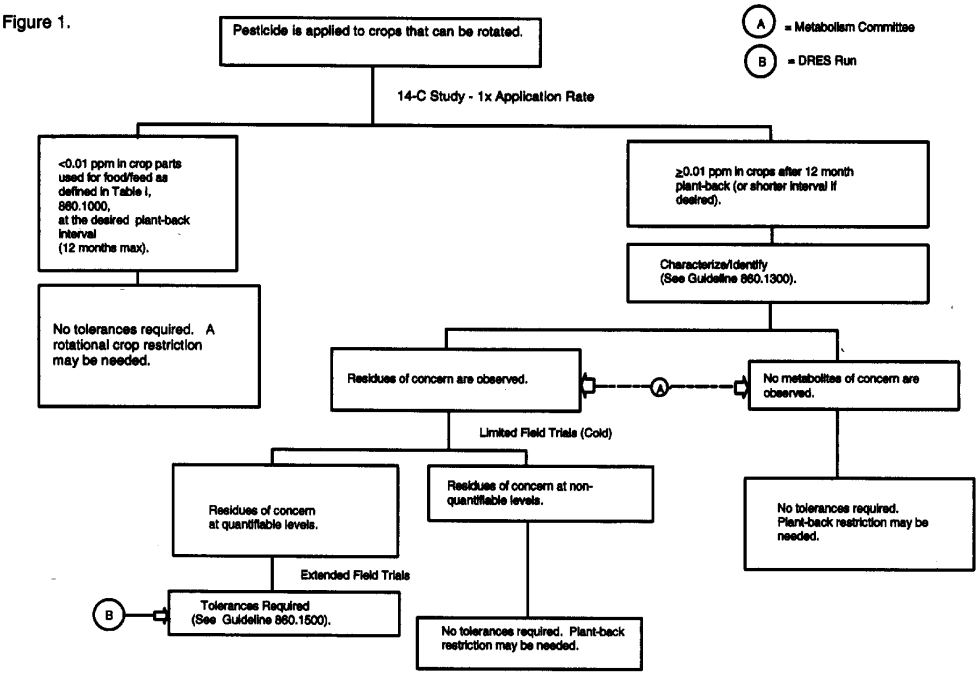
(1) Historical.

Studies on confined rotational crops are conditionally required under 40 CFR 158 for uses of pesticides on terrestrial food crops and aquatic food crops. A rotational crop use is any field-vegetable crop use, aquatic crop use or any other site use on which it is reasonably foreseeable that any food or feed crop may be produced after application of a pesticide. The purpose of these studies is to determine the nature and amount of pesticide residue uptake into rotational crops. The confined study uses radioactive material applied to a small plot. Results of these ‘‘hot’’ studies are used to determine whether field studies (using non-radioactive pesticide) are needed. Based on these data appropriate crop rotation restrictions (time from application to planting of rotational crop) may be established and the need for tolerances on the rotated crops determined.

(2) Scientific considerations.

Confined rotational crop studies are essentially metabolism studies; therefore, guideline 860.1300, Nature of the residue plants, livestock, should be consulted before conducting a confined rotational crop study. (It should be noted that, in the case of confined rotational crop studies, the application rate is 1X, not an exaggerated rate.) This section will refer frequently to that document when discussing various phases of the subject experiments. A flow diagram describing the approach discussed in this guideline is provided in Figure 1.

Figure 1.



The following should be considered when a confined rotational crop study is to be conducted. The test material should be the pure active ingredient radiolabeled (PAIRA) with 14C in a non-labile position (e.g., in a ring). The parent compound only should be applied to the appropriate soil type (usually a sandy loam) at the maximum seasonal label rate (1X) and the required three rotated crops (small grain [e.g., wheat, barley], leafy vegetable [e.g., spinach, lettuce], and root crop [e.g., radish, table beets, carrots]) should be planted at appropriate soil aging intervals (e.g., 1, 4, 7 or 9, and 12 months). The representative root crop should not be a bulb vegetable such as onions or garlic. It is acceptable to substitute soybeans for a leafy vegetable due to the importance of this crop in rotational practices. Growing a primary crop in the soil during the aging period is not precluded provided the soil is treated prior to planting. Sampling of the soil is not required and need only be performed at the Registrant's discretion. The three rotated crops should be harvested and the appropriate plant parts (see Table I in OPPTS guideline 860.1000) should be sampled and combusted to determine the total radioactive residue (TRR). At this point, if each of the three crops demonstrate a TRR of <0.01 ppm in edible portions at one of the plantback or soil aging intervals then the Chemistry Branches will conclude that no further work and no tolerances are needed. An appropriate rotational crop restriction can be set at the shortest interval where no TRR is (replacement note for greater than less than symbol) 0.01 ppm, provided that the Registrant is willing to place this interval on the label. If the TRR is <0.01 ppm in all three crops at the one month interval, then no plantback restriction will be needed on the label. If, however, in the three confined studies, the minimum intervals at which the TRR is <0.01 ppm differ, then the rotational crop restrictions will be set at the

interval appropriate to each tested crop group with the longest interval being applied to all other (untested) rotated crops. The following example should be considered:

The TRR for leafy vegetables is <0.01 ppm at the 1 month plantback interval, the root crop TRR is <0.01 ppm at the 4 month interval and the grain crop TRR is <0.01 ppm at the 9 month interval. The rotational crop restrictions would be 1 month for leafy vegetables, 4 months for root crops and 9 months for small grains and all other rotated crops. It is the Registrant's prerogative to perform additional confined rotational crop studies on other crops to establish less restrictive intervals based on levels of radioactivity.

In rare cases, the toxicologists may have concerns regarding the presence of a pesticide or metabolite at levels <0.01 ppm. Determination of the presence (or absence) of specific metabolites of concern at levels <0.01 ppm may be required in these cases.

If any of the plants in the confined studies exceed the trigger value (0.01 ppm) at the 12 month interval, then the nature of the residue in those test crops having a TRR >0.01 ppm must be determined. The registrant is referred to the guidance provided in guideline 860.1300, Nature of the residue - plants, livestock (however, see also the above comment regarding the application rate for confined rotational crop studies) for a description of the procedures which need to be followed to accomplish this determination.

If any one of the three crops shows <0.01 ppm at a given interval but the Registrant desires a shorter interval on the label for that crop where the TRR is >0.01 ppm, then the composition of the TRR in that rotated crop (at the desired interval) should be determined as described above for the crop parts where the trigger value (i.e., 0.01 ppm) was exceeded. If several samples of the crop are available at the desired interval, the sample having the highest TRR should be utilized. In either of the above cases, this information is needed in order that the Agency can make a conclusion as to whether the residue is an inadvertent residue of no concern or whether cold (i.e., not radiolabeled) field trials are needed to make that determination.

If the metabolism in rotated crops appears to be different than that in the primary crop, that is, if different metabolites are observed in rotated crops than in primary crops, the Agency will make a determination as to whether the different rotational crop metabolites are of concern at the levels observed. If necessary, the HED Metabolism Committee will be consulted.

The following are examples of the situations described above:

The primary (target) crop metabolism studies indicate that the parent and metabolites A, B, C, D and E are present in the plant. The Agency decides that only the parent and metabolite B need to be regulated in the tolerance

expression. The following three scenarios might be encountered regarding rotational crops:

(i) The confined rotational crop studies indicate that the TRR is >0.01 ppm and that parent and metabolites A, B, C and D are present. Limited rotational crop field trials will normally be required with analysis for parent and metabolite B if it is determined that these residues could be present at detectable levels. If, however, metabolites A, C and D are present at much higher levels in the rotational crops than in the primary crop, the HED Metabolism Committee may be consulted as to whether the other metabolites need to be quantitated.

(ii) The confined rotational crop studies show that the TRR is >0.01 ppm and that the radioactive residue consists of only metabolites D and E. In this case the Agency would normally conclude that this is an inadvertent residue of no concern situation and no field trials would be required. A rotational crop restriction (i.e., plantback interval) may be necessary. As above however, if metabolites D and E are present at much higher levels in the rotational crops than in the primary crop, the HED Metabolism Committee may be consulted as to whether these metabolites need to be quantitated.

(iii) The confined rotational crop studies indicate that the TRR is >0.01 ppm and that there is no parent present but that the major portion of the TRR consists of a new metabolite F. This will require a decision, as to whether there is toxicological concern over the new metabolite. At this point the HED Metabolism Committee may be consulted for an expedited decision. If it is concluded that the metabolite is of concern at the levels likely to be present, then F should be analyzed for in the limited rotational crop field trials. If it is decided that F is of no concern then, as in (ii) above, this is an inadvertent residue of no concern situation and no field trials are necessary. However, a rotational crop restriction may be necessary.

It is recommended that the confined studies be submitted to the Agency as soon after completion as possible, so that the Agency can make a conclusion as to whether there is a potential inadvertent residue of concern (i.e., will limited field trials be needed?). This will allow the registrant to design the field trials in a more efficient manner (i.e., what compounds require analysis in the field trials).

(c) Test standards.

(1) Test substance. This study shall be conducted using the radioactively-labeled analytical grade of the active ingredient. If multiple ring structures are present, separate studies reflecting labeling of each ring will normally be required.

(2) Test procedures.

(i) This study should be performed using a sandy loam soil which has been treated with the test substance applied at a rate equivalent to the maximum seasonal rate (1X) under actual field use conditions. However, if the label instructions of the product limit its use to one soil type other than the sandy loam, then the study should be run with the soil type specified on the label. In either case, the soil should not be sterilized. Also, if the maximum seasonal application rate can only be attained by multiple treatments under actual use conditions (e.g., many foliar insecticides and fungicides), the radiolabeled material may be applied to the soil in a similar manner. In other words, the entire dose for the season need not be applied at once for such active ingredients.

(ii) The study may be performed either in a greenhouse or on an outdoor plot or container. Following application to the soil the pesticide may be incorporated into the soil if the product label so instructs or this represents typical agricultural practice.

(iii) Following soil treatment, the pesticide should be aged under aerobic conditions in the soil for a time approximating the anticipated agricultural practice (e.g., 1 year for crops rotated the following year, 120 days for crops rotated immediately after harvest, and 30 days for assessing circumstances of crop failure). Growing a primary crop in the soil during the aging period is not precluded provided the soil is treated prior to planting.

(iv) Crops planted in the treated and aged soil should include those expected in the proposed rotational schedule and, where possible, be representative of each of the following crop groupings: root and tuber vegetable (e.g., radish, table beets, carrots), small grain (e.g., wheat, barley), and leafy vegetable (e.g., spinach, lettuce). Soybeans may be substituted for a leafy vegetable due to the importance of this crop in rotational practices. The selected crops shall be analyzed for residues at appropriate harvest intervals. (Residue analyses should be performed on selected crops at multiple intervals if both immature and mature crops are normally harvested in the course of usual agricultural practices.)

(d) Reporting and evaluation of data. In addition to the applicable reporting requirements specified in OPPTS 860.1000, the following data should be reported:

(1) The registrant should characterize and, when feasible, identify and provide analytical values for significant residues in the crops tested. Significant residues include parent compound, closely-related degradates, metabolites and/or their conjugates in the crop. In cases where identification of residues is not feasible due to insufficient sample, then pooling of samples obtained from replicate experiments conducted simultaneously should be carried out to enable residue identification to be achieved. From the results of this study, the Agency will determine whether additional

studies to measure the accumulation of pesticide residues in rotated crops under actual field conditions are needed. If such field studies are needed, the registration applicant will need to determine whether to conduct the limited field studies described in OPPTS 860.1900 (two trials each on representative crop(s)) or to carry out a complete set of crop field trials as described in OPPTS 860.1500 necessary to support the establishment of a tolerance in the rotated crop(s).

(2) Depending on the crop tested, separate analyses should be conducted on those portions of the plant considered to be raw agricultural commodities (see Table I in 860.1000). However, even if the aerial portion for the particular root crop is not in Table I, both the aerial and root portions of root crops should be analyzed.

(3) There is no need to account for all applied radioactivity since soil analyses are not required.

(4) A description of the growing conditions should be reported. If the study is conducted outdoors, rainfall data, temperature monitoring data, and general climatic conditions should be reported for the test period.

(e) Format of data report. The following describes the order and format for a study report item by item.

(1) Title /cover page. Title page and additional documentation requirements (i.e., requirements for data submission and statement of data confidentiality of data) if relevant to the study reported should precede the content of the study formatted below. These requirements are described in PR Notice 86-5 (see paragraph (f)(2)).

(2) Table of contents. The Table of Contents must follow the title, data confidentiality, and GLP pages. This page should indicate the overall organization of the study, including tables and figures.

(3) Abstract. This section should contain the overall summary of the study addressing the following points:

(i) The chemical (use the same name throughout the report), the formulation and the mode of application. Structures of the chemical and metabolites may be included in this section.

(ii) Maintenance of the treated plot.

(iii) A table similar to the following with an appropriate title:

Days after Application	Residues (ppm)		
	Total	Parent	Metabolites[1] plant tissue
.....			

[1]Metabolites may need to be named and quantitated individually.

(iv) A discussion of unexpected problems (such as technical difficulties or unusual weather) which necessitated deviations from the intended test protocol and a description of the effects of these deviations on the results of the study; and

(v) Provide a name and a phone number of a contact person in the event the reviewer has technical questions about the study. [This is optional. However, providing this information will facilitate efficient review in case of questions.]

(4) Introduction. This section should open with a description of the purpose of the study, what requirement it is intended to satisfy and (if applicable) how it supports the position of the registrant. Background and historical information relative to the study should be placed in this section.

(5) Materials/methods. The registrant may elect to describe materials and methods in separate sections or combine into a single section. The following format combines the two into one section. This section should be in narrative form. All details (including drawings and photographs) with regard to the materials, equipment, experimental design, test plots or containers, procedures used in conducting the study, and of different phases of the study should be placed in this section. In addition, the following are to be included, when appropriate:

(i) Chemical. Provide the purity of the material, its activity in Curies/mole, disintegrations per minute per gram (dpm/g), and the site of radiolabeling.

(ii) Site.

(A) If test plots are used:

(1) Provide a map describing location, topography and size, and location and size of any control plots in relation to the test plot; and an indication of whether the test plot contains a subsurface drainage system;

(2) Describe the means by which the test material is confined in the areas surrounding the test plantings - e.g., aluminum pipe sunk in the ground;

(3) Provide the soil characteristics (% sand, % silt, % clay, % organic matter, pH, cation exchange capacity, and moisture capacity) of the plot;

(4) Provide a complete record of daily temperature, daily rainfall and pan evaporation data throughout the study and how they compare to average temperature and rainfall at the test site based on records from the nearest weather station; and

(5) Include crop and pesticide use history on the plot for the three year period preceding the study.

(B) If test containers are used, provide information on the size of the containers; amount of soil, its type and characteristics as detailed in ''A'' above, and other distinctive details.

(iii) Test method.

(A) General.

(1) The date and technique of plot or container preparation prior to pesticide application;

(2) A description of how and when the pesticide was applied; the ambient conditions at the time of application; the application rate and the application technique; also, similar descriptions for each of any additional applications made; information on how much pesticide was applied in comparison to actual use rates; and if application technique differed from label recommendations;

(3) The identity of the treated crop, if applicable, and a description of how and when the treated crop was planted;

(4) A description of any post-treatment crop maintenance such as use of fertilizers and other pesticides, irrigation (when applied, how much, and its source), tilling, weeding, etc.;

(5) A description of the crop sampling technique, procedure and devices used; and the date of harvest of the treated crop;

(6) A description of what was done to the plot after harvest of the treated crop before planting of the rotational crop, during planting of the rotational crop, and during its growth;

(7) Identity of the rotational crops planted should be placed in this section. Also, provide a description of the procedure used in planting the rotational crops; the number of days between treatment of the initial crop with the pesticide and planting of the rotational crop; and a description of all procedures used in the maintenance of the rotational crops (as done for the treated crop), sampling method and how many samples/replicates were taken. All dates should be provided in terms of ''days from pesticide application.''

(8) A description of the handling of the crop samples from the time of taking of the samples until analysis with special attention to the conditions under which they were stored and the thawing procedure (if frozen); in addition, the storage stability data to be used in determining if the pesticide residues are stable under the storage conditions; and the dates the samples were stored/frozen, thawed, and analyzed;

(9) Information on how long samples will be retained and under what conditions they will be retained (in the event additional analytical work is necessary); and

(10) An elaboration on any difficulties or special problems that arose during the study which necessitated deviation from the intended test protocol and on the effects the deviations had on the results.

(B) Analytical method.

(1) The full description of each method used in this study should be placed in this section. Note that methods for degradation products, when appropriate, are included. This section should also include the method validation data, recovery and limit of detection data, quality control procedures and results, sample chromatograms, and sample calculations. The detailed description of the procedures used in preparation and handling of the sample throughout the method should also be placed here;

(2) The identity of the instrumentation, equipment and reagents used and the operating conditions of the instrumentation;

(3) Figures/photographs of any special equipment used in the methods; and flow diagrams of particularly complex extraction/clean-up procedures are to be included here; and

(4) The results of analyses of all crop samples.

(6) Results/discussion.

(i) This section should contain the scientific results of the study, for instance;

(A) Narrative and tables describing the steps taken in determining the pesticide residues in the crop samples in addition to the graphical presentations of the data (accompanied by the tables of the actual values from which the graphs were constructed);

(B) Results of the analysis of any control plots. The registrant should note that the crop samples for both control and treated plots and/or containers are to be analyzed for levels of radioactive residues;

(C) Significant residues should be characterized further, with special attention to known degradates from plant metabolism, soil metabolism, hydrolysis and photolysis.

(ii) This section should contain the table of structures and chemical names/designations for the parent compound and degradation products discussed in the study.

(7) Conclusion. This section should contain the discussion of the nature, magnitude and toxicological significance of the residues of parent, metabolites and degradates found in the rotational crops.

(8) Certification.

(i) Signatures of each of the senior scientific personnel responsible for the study; and

(ii) Certification by the registrant that the report is a complete and unaltered copy of the report provided by the testing facility (except for title page changes required by PR Notice 86-5).

(9) Tables/figures. It is recommended that tables and figures be numbered using arabic numerals for figures and roman numerals for tables.

(10) References.

(11) Other. At the registrant's option, reprints of methods and other studies, raw data, copies of relevant letters/memos and material which will help support the registrant's conclusions, but do not fit in any of the other sections, should be placed in an appendix.

(f) References. The source material for this guideline is taken directly from the following set of documents.

(1) U.S. Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision O, Residue Chemistry. EPA Report No. 540/9-82-023, October, 1982, (Available from National Technical Information Service, Springfield, VA).

(2) U.S. Environmental Protection Agency, Pesticide Registration Notice PR 86-5, Standard Format for Data Submitted under the FIFRA and Certain Provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA), May 3, l986.