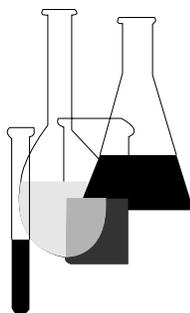




Product Properties Test Guidelines

OPPTS 830.1000

Background for Product Properties Test Guidelines



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.*).

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OPPTS 830.1000 Background for product properties test guidelines.

(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 Toxic Substances Control Act (15 U.S.C. 2601).

(2) **Background.** (i) The source materials used in developing this harmonized OPPTS document are the OPP test guidelines Series 60 through Series 64 (Pesticide Assessment Guidelines, Subdivision D, Product Chemistry, EPA report 540/9–82–018, October 1982).

(ii) This guideline presents an overview of the 830 Product Properties series of test guidelines and provides general guidance on testing procedures and data submission.

(b) **Purposes of product chemistry guidelines.** (1) This series of test guidelines describes protocols which may be used to perform product chemistry testing to support the registration and reregistration of pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). It is a nonregulatory companion to 40 CFR Part 158, Data Requirements for Registration. Circumstances when testing is required are encoded explicitly in part 158 and the user should use that regulation along with the test guidelines in the 830 series.

(2) These guidelines supersede the earlier product chemistry guidelines published as Subdivision D of the Pesticide Assessment Guidelines and provide harmonization, where possible, with similar guidelines published by the Organization for Economic Cooperation and Development (OECD). The earlier guidelines, Subdivision D, had four sections: Series 60—General Information, Series 61—Product Identity and Composition, Series 62—Analysis and Certification of Product Ingredients, Series 63—Physical and Chemical Characteristics, and Series 64—Other Product Chemistry Requirements. In the revised guidelines, Series 60 is replaced by this guideline, OPPTS 830.1000. Series 61 and 62 are combined in one group titled “Group A—Product Identity, Composition, and Analysis.” Physical and chemical characteristics remains a separate section, titled “Group B—Physical/Chemical Properties,” in the new guidelines. The single Series 64 guideline, 64–1 Submittal of Samples, has been placed in Group A as OPPTS 830.1900. Table 1 provides a listing of the OPPTS test guidelines and shows the correlation between the guideline numbers from Subdivision D and the new guideline numbers. It should be noted that one new test guideline (OPPTS 830.7050 UV/visible absorption) has been added to the Physical/Chemical Properties group.

Table 1.—Listing of OPPTS Test Guidelines and Correlation with Subdivision D Test Guidelines

Guideline title	Old guideline number	New guideline number
Group A—Product Identity, Composition, and Analysis		
Product Identity and composition	158.155	830.1550
Description of materials used to produce the product	158.160	830.1600
Description of production process	158.162	830.1620
Description of formulation process	158.165	830.1650
Discussion of formation of Impurities	158.167	830.1670
Preliminary analysis	158.170	830.1700
Certified limits	158.176	830.1750
Enforcement analytical method	158.180	830.1800
Submittal of samples	64–1	830.1900
Group B—Physical/Chemical Properties		
Color	63–2	830.6302
Physical state	63–3	830.6303
Odor	63–4	830.6304
Melting point/melting range	63–5	830.7200
Boiling point/boiling range	63–6	830.7220
Density/relative density/bulk density	63–7	830.7300
Water solubility: Column elution method; shake flask method	63–8	830.7840
Water solubility, generator column method	63–8	830.7860
Vapor pressure	63–9	830.7950
Dissociation constant	63–10	830.7370
Petition coefficient (<i>n</i> -octanol/water), shake flask method	63–11	830.7550
Petition coefficient (<i>n</i> -octanol/water), generator column method	63–11	830.7560
Petition coefficient (<i>n</i> -octanol/water), estimation by liquid chromatography	63–11	830.7570
pH	63–12	830.7000
Stability to normal and elevated temperatures, metals and metal ions	63–13	830.6313
Oxidation/reduction: chemical incompatibility	63–14	830.6314
Flammability	63–15	830.6315
Explosibility	63–16	830.6316
Storage stability	63–17	830.6317
Viscosity	63–18	830.7100
Miscibility	63–19	830.6319
Corrosion characteristics	63–20	830.6320
Dielectric breakdown voltage	63–21	830.6321
UV/visible absorption	None	830.7050

(3) The Agency intends that the guidelines provide meaningful information to applicants, registrants, and the general public regarding the product chemistry data requirements for registration of a pesticide. Such guidelines should enable the members of the pesticide industry to use test methods acceptable to the Agency and to anticipate the costs as well as the time involved in preparation of an application for registration. Toward these ends, these guidelines specify the standards for acceptable testing and the information required in a test report. The guidelines also suggest circumstances under which an applicant should consult with the Agency before initiating a test. In addition, the guidelines provide acceptable protocols for conducting the required testing.

(4) The Agency believes that adherence to these guidelines will result in reliable data to support applications for registration, and will accelerate and upgrade the Agency’s review and evaluation of registration applications.

(c) **Useful terms.** The Administrator is authorized by FIFRA to regulate pesticide products distributed in commerce. The term “*pesticide product*” is defined in 40 CFR 152.3(s) as a pesticide in the particular form (including composition, packaging, and labeling) in which the pesticide is, or is intended to be, distributed or sold. The term includes any physical apparatus used to deliver or apply the pesticide if distributed or sold with the pesticide. All pesticide products can be classified into three categories:

“Technical grade of the active ingredient (TGAI),” “manufacturing-use products (MP),” and “end-use products (EP).” “*Technical grade of the active ingredient,*” which is used interchangeably with “*technical chemical,*” means a material containing an active ingredient which contains no ingredient, other than one used for manufacture or purification of the active ingredient and which is produced on a commercial or pilot-plant production scale (whether or not it is ever held for sale). A “*manufacturing-use product*” is any pesticide product other than an end-use product. A manufacturing-use product may consist of the technical grade of the technical grade of the active ingredient only, or may contain inert ingredients, such as stabilizers or solvents. Manufacturing-use products are, as the term implies, used in the production of end-use products, primarily through reformulation, i.e., mixing the manufacturing-use product with different chemical substances such as solvents or diluents. An “*end-use product*” is defined as a pesticide product whose labeling includes directions for use of the product (as distributed or sold, or after combination by the user with other substances) for controlling pests or defoliating, desiccating or regulating of plants and does not state that the product may be used to manufacture or formulate other pesticide products.

Formulation means the process of mixing, blending, or dilution of one or more active ingredients with one or more other active or inert ingredients, without an intended chemical reaction, to obtain a manufacturing-use product or an end-use product. All pesticides are composed of one or more substances. For regulatory purposes the substances are classified either as active ingredients, intentionally-added inert ingredients, or impurities. The term “*active ingredient*” means any substance (or group of structurally similar substances, if specified by the Agency) that will prevent, destroy, repel or mitigate any pest, or that functions as a plant regulator, desiccant, or defoliant, within the meaning of FIFRA section 2(a). In short, the active ingredients in pesticides are the substances which directly produce the intended pesticidal effect.

Pesticides contain “*impurities,*” which are defined as any substance (or group of structurally similar substances if specified by the Agency) in a pesticide product other than an active ingredient or an inert ingredient, including unreacted starting materials, side reaction products, contaminants, and degradation products and pesticide active ingredients other than those intended for that product.

The Agency has become increasingly concerned about impurities in pesticides, particularly impurities associated with an active ingredient. The term “*impurity associated with an active ingredient*” means:

(1) Any impurity present in the technical grade of the active ingredient (e.g., a substance carried over from a beginning material, or from an intermediate, and impurities formed through side reactions or by degradation of the active ingredient).

(2) Any impurity which forms in a pesticide product through reactions between the active ingredient and any other component of the product or packaging of the product.

“*Inert ingredient*” means any substance (or group of structurally similar substances if designated by the Agency), other than an active ingredient, which is intentionally included in a pesticide product. Intentionally-added inert ingredients include wetting agents, emulsifiers, surfactants, aerosol propellents, diluents, solvents, stabilizers, and the like.

The term “*integrated system*” (formerly called “integrated formulation system”) means a process for producing a pesticide that:

(1) Contains any active ingredient derived from a source that is not an EPA-registered product; or

(2) Is a result of a reaction between an EPA-registered product and other chemicals to form a new active ingredient; or

(3) Contains any active ingredient that was produced or acquired in a manner that does not permit its inspection by the Agency under FIFRA section 9(a) prior to its use in the process.

In other words, the term “*integrated system*” includes, but is not limited to, any process for producing a pesticide product that would contain an active ingredient which is not present as the result of using a registered pesticide product. End-use products not produced by an integrated system are unlikely to contain any impurities associated with an active ingredient other than those impurities already identified in connection with registration of a product used to make such an end-use product. The purpose, then, of including this definition is to distinguish between the two types of end-products (those produced by an integrated system and those which are not), and to impose less stringent requirements on products which are not produced by such a system.

“*Nominal concentration*” means the amount of an ingredient which is expected to be present in a typical sample of a pesticide product at the time the product is produced, expressed as a percentage by weight.

The term “*starting material*” (formerly called “beginning material”) means a substance used to synthesize or purify an active ingredient (or the practical equivalent of the technical grade ingredient if the active ingredient cannot be isolated).

(d) **General considerations.** Data submitted to meet the requirements for product chemistry fall into two major categories: Information on product identity, composition, and analysis and information on specific physical and chemical characteristics of pesticide chemicals and products.

(1) **Product identity, composition, and analysis.** (i) These data include information about the product identity and composition (OPPTS 830.1550); description of materials used to produce the product (OPPTS 830.1600); description of production process (OPPTS 830.1620); description of the formulation process (OPPTS 830.1650); the discussion on formation of impurities (830.1670), the results of preliminary analysis of product samples (OPPTS 830.1700); the explanation of how the certified limits were determined (OPPTS 830.1750); the description of the enforcement analytical method (830.1800); and instructions on submittal of samples to the Agency (OPPTS 830.1900) These data support the conclusions expressed in the Confidential Statement of Formula (CSF). Virtually all of the information submitted for this section will be trade secret and confidential business information (CBI).

(ii) Product composition data are used in several ways. First, the Agency reviews the composition of a product to determine whether the product contains any ingredient in an amount which may cause unreasonable adverse effects on the environment. This review is based on information available to the Agency from the public literature and its own files about the toxicity and environmental effects of ingredients. This is the primary use of product composition data.

(iii) The Agency also uses product composition data when reviewing applications for conditional registration. FIFRA section 3(c)(7)(A) authorizes the conditional registration of products which are “‘identical or substantially similar to any currently registered pesticide * * * or differ only in ways that would not significantly increase the risk of unreasonable adverse effects on the environment * * * ’”. In nearly every case, this determination involves an examination of an application and a comparison with the composition of currently-registered products.

(iv) Finally, the Agency compares data on product composition with information on the composition of materials used in toxicity tests and other kinds of studies. This comparison indicates which ingredients in a pesticide product have been evaluated by a particular study, and might lead to a conclusion that another study is needed.

(v) Based on its conclusions concerning the environmental characteristics and toxic properties of the pesticide, the Agency can impose appropriate use restrictions, labeling requirements, special packaging requirements, or other needed requirements.

(2) **Physical and chemical characteristics.** (i) Data on the physical and chemical characteristics of pesticide chemicals and products are presented in OPPTS guidelines 830.6302 through 830.7950. Some characteristics confirm or provide supportive information on the identity of ingredients and products. This is particularly true for such properties as color, odor, physical state, melting and boiling points, density, solubility, vapor

pressure, and pH. In addition, such data provide information which is useful in reviewing the manufacturing or formulating process used to produce the chemical or product. Marked raising or lowering of pH, melting or boiling points, vapor pressure, density, or solubility, for example, may provide evidence of significant changes in manufacture or formulation, and could indicate the need to investigate product composition further.

(ii) Such information as color, odor, physical state, pH, and viscosity is also needed by the Agency to respond to emergency requests for identification of unlabeled pesticides involved in accidents or spills. Physicians, hospitals, and poison control centers also request such information from time to time when apparently-poisoned victims (or their families or acquaintances) cannot identify specific pesticide products to which the victims have been exposed. This has often been the case when pesticides are removed from their original containers.

(iii) Physical and chemical characteristics data are used directly in hazard assessment. These include pH, stability, oxidizing and reducing action, flammability, explosibility, storage stability, corrosion characteristics, and dielectric breakdown voltage. EPA requires a study of the corrosion characteristics of a pesticide to evaluate the effect of the product formulation on the container; if the pesticide is highly corrosive, then lids, liners, seams, or container sides may be damaged causing the contents to leak during storage, transportation, handling, or use. The storage stability study provides data on change (or lack of change) in product composition over time; if certain ingredients decompose, obviously other new chemicals are formed whose toxicity and other characteristics need to be considered. This situation is also true, to some extent, for data needed on stability of technical chemicals. Depending on the results of those tests, EPA may impose requirements for precautionary label statements.

(iv) Also, certain data in this series are needed as basic or supportive evidence in initiating or evaluating studies required by other disciplines. For example, the octanol/water partition coefficient is used as a criterion in determining whether certain fish and wildlife toxicity studies (in OPPTS guideline series 850) must be conducted. Data on vapor pressure are used directly in determination of reentry intervals for products that may be used in situations where residues in air pose a potential hazard (OPPTS guideline series 835). Data on viscosity and miscibility provide supportive information on tank mix products (examined more extensively in OPPTS guideline series 835) and spray application instructions (of special concern in guideline series 810). Determination of the UV/visible absorption spectrum of a pesticide provides some indication of the wavelengths at which the compound may be susceptible to photochemical degradation. Since photochemical degradation is likely to occur in both the atmosphere and aquatic environment, spectra appropriate to these media will provide information concerning the need for further persistence testing .

(e) **Discussion of the guidelines—(1) Product identity, composition, and analysis test guidelines—(i) OPPTS 830.1550 Product identity and composition.** (A) The most important requirements in the product chemistry guidelines are contained in OPPTS 830.1550, Product identity and composition. This guideline discusses the submission procedures for the statement of formula identifying each active ingredient, each intentionally-added inert ingredient, and, in certain cases, impurities that may be present in the product while it is being distributed in commerce. The purposes of the requirements in this guideline are to obtain a comprehensive listing of the ingredients that may be present in a product and the amounts of such ingredients and to assemble in one section of an application all of the major types of identifying information on a product and its ingredients. The composition information will be used primarily in subsequent evaluations of the safety of the product. The identifying information will be used as an aid in locating data in the public literature concerning the human health and environmental properties of the product and/or its ingredients. Identification of an ingredient calls for a variety of information: For all ingredients, the chemical name and Chemical Abstracts Service (CAS) number for active and intentionally-added inert ingredients, the purpose or function of the ingredient and for active ingredients, the molecular, structural, and empirical formula, the molecular weight (or range), as well as other means of identification.

(B) In addition to identifying the ingredients in the product, the applicant must also provide certified limits for the ingredients listed in the statement of formula. Upper and lower certified limits must be established for each active ingredient and each intentionally-added inert ingredient. In addition, for some types of products, an upper certified limit must be established for certain impurities. The upper certified limit is the maximum (and the lower certified limit is the minimum) amount of the ingredient that will be present in the product at any time while it is in commerce.

(C) This guideline requests an applicant to identify the product by the product name and trade name(s) (if different) and the company code number assigned to the product. The Statement of Formula is required as a means of identifying the ingredients in products. Submission of a Confidential Statement of Formula (CSF) is insufficient. For end-use products, this information should be more detailed than what is required on the CSF, in that various chemical names, and structural formulas and molecular weights for ingredients should be given. For technical materials, impurities identified during development should be identified and quantitated and the methods used to do so should be explained. The quantitative information may need to be revised after the preliminary analysis (see OPPTS 830.1750).

(ii) **OPPTS 830.1600 Description of materials used to produce the product.** (A) Most of the other product chemistry guidelines are intended to produce data to support the information contained in the statement of

formula. The first of these data requirements are contained in OPPTS 830.1600, concerning descriptions of beginning materials and the manufacturing process.

(B) The most basic pieces of information needed to determine the composition of a pesticide product are the identity and the composition of the materials used to produce the product. An applicant is required to identify each beginning material used to produce his product and to supply certain information on the beginning material. Specifically, the applicant is required to submit a copy of available technical specifications by which the supplier of a beginning material describes its composition, properties, and/or toxicity as well as any other information available to the applicant concerning the composition and properties of the beginning material. If a beginning material is a registered pesticide product it is sufficient simply to identify the product by its registration number. An applicant is required to submit only the information (of the types specified) which is available to the applicant. An applicant is not required to perform periodic chemical analyses of his beginning materials.

(C) The description of the manufacturing process should be submitted in detail. If a registrant is uncertain about what level of detail to include, the Agency suggests that more specific is better. Equipment descriptions are needed as well as process flow diagrams, reaction conditions and details of the chemical reactions intended to occur. While registrants or applicants are not required to analyze starting materials, any available information on purity of starting materials should be submitted. A schematic diagram/brief description of the production process will suffice if the pesticide is still in pilot scale production and an experimental use permit is being sought.

(D) The level of detail for end-use products is generally less than for the technical grade of the active ingredient and manufacturing-use products, since impurities and side reactions rarely occur as a result of the formulation (mixing) process, except for N-nitroso contamination (see OPPTS 830.1670). Copies of Material Safety Data Sheets for all starting materials should be submitted. End-use products, except for those with potential N-nitroso contamination, may warrant a paragraph, while technicals typically require multiple pages.

(E) A description of quality control processes, as well as quality control data, should be submitted. If several different groups oversee quality control, a description of each and the data from each should be provided.

(iii) **OPPTS 830.1620 Description of production process.** (A) OPPTS 830.1620 specifies the kind of information which should be contained in this description of the production process used to make the product. Among other things, the description should include: A statement of the order in which beginning materials are added and their amounts; a

description of the conditions controlled during the production process; a description of any purification procedures; and a description of any quality control measures. In addition, the applicant must provide a flow chart showing the intended chemical reactions occurring during each step of the process. A schematic diagram/brief description of the production process will suffice if the pesticide is still in pilot scale production and an experimental use permit is being sought.

(B) Based on EPA experience reviewing N-nitrosamine analyses of many products, especially dimethylamine salts, the Agency no longer requires analysis for N-nitroso contaminants in products containing:

(1) Secondary and tertiary alkylamines or alkanolamines.

(2) Representative quaternary ammonium compounds (as defined by agreement between EPA and the International Sanitary Supply Association) provided that:

(i) Nitrosation or nitration does not occur in an early step in synthesis.

(ii) Nitrites, nitrates, or other nitrosating agents are not added to the product or packaging.

The Agency will continue to require analysis for N-nitroso contaminants in products containing dinitroanilines. Two representative batches of each product are to be sampled. A total of two samples from each batch are to be analyzed. One of these samples should be taken and analyzed as close after the time of production as is practical and determinable. Three months following the initial analyses, one additional sample must be taken and analyzed from the same batch of product stored at normal storage temperature and conditions. The maximum nitrosamine contamination allowed is ≤ 1 ppm based on the limit of quantitation (LOQ) of the analytical method.

(iv) **OPPTS 830.1650 Description of formulation process.** (A) If the product is the result of a formulation process, the applicant should provide (unless the product consists solely of a technical grade of the active ingredient) the following information: A general description of the process; identification of the ingredients used in the formulation; a description of the process equipment and process conditions; and a description of any quality control measures. A schematic diagram/brief description of the production process will suffice if the pesticide is still in pilot scale production and an experimental use permit is being sought.

(B) Together, the descriptions of the materials used to produce the product and the production/formulation process identify the major factors affecting the composition of a pesticide product. Agency chemists can review this data along with information contained in other guidelines to de-

termine whether the applicant's product will contain the ingredients and conform to the certified limits listed in the statement of formula.

(v) **OPPTS 830.1670 Discussion of the formation of impurities.**

(A) OPPTS 830.1670 addresses the applicant's submission of a discussion based on chemical theory of the impurities that may be present in his pesticide products and to explain how such impurities may be formed. Applicants are required to address impurities which either have been detected by analysis of samples of the product or are expected to be present in quantities equal to or greater than 0.1 percent of the product or at lower concentrations in the case of impurities of toxicological concerns.

(B) EPA expects this discussion to serve several functions. The Agency will learn what kinds of impurities the applicant expects will be present in his product as it is distributed in commerce. EPA can independently evaluate this information to determine whether other impurities might be present in the product. In addition, the thoroughness of the theoretical discussion can be an indication of completeness of the sample analysis requirements contained in 40 CFR 158.170.

(C) This guideline states expressly that the discussion is to be based on the information concerning beginning materials and the production/formulation process described in OPPTS guidelines 830.1620 and 830.1650. It also specifies the particular kinds of chemical reactions which must be considered and discussed. Different requirements in this latter respect are established for end-use products not produced by an integrated system and all other products (end-use products produced by an integrated system and manufacturing-use products). Applicants seeking to register end-use products not produced by an integrated system are subject to less stringent requirements since the impurities associated with an active ingredient in such a product will almost always be the impurities present in the pesticide active ingredient used to formulate their products. Thus, for these applicants, the theoretical discussion should focus on possible reactions between the active ingredient and other ingredients in the pesticide when such information is known. Applicants seeking to register other kinds of products must discuss the possibility of chemical reactions involving other substances, e.g., reactions between intentionally-added inert ingredients and packaging. If the pesticide is still in pilot-scale production and an experimental use permit is sought, a discussion of impurities will be submitted to the extent this information is available.

(vi) **OPPTS 830.1700 Preliminary analysis.**

(A) OPPTS 830.1700 is intended to allow an applicant to confirm the conclusions reached in the theoretical discussion. This guideline requests applicants to report the results of analyses of five or more production batches of the product. The analyses must be designed to measure the amount of active ingredient present in the product and to identify and quantify (if present) any impurity associated with an active ingredient which is expected (based on the theo-

retical discussion) to constitute 0.1 percent or more of the product. On a case-by-case basis, EPA may require applicants to analyze product samples for other ingredients or to provide identifying spectral data.

(B) The requirements for analysis of product batches apply to manufacturing-use products (including those containing solely the TGAI) and end-use products produced by an integrated system. Data on other end-use products will be required on a case-by-case basis. For pesticides in the development stage, a rudimentary product analytical method and data will suffice to support an experimental use permit. Once again, end-use products not produced by an integrated system are subject to less stringent requirements. Applicants seeking to register such products will be required to provide the results of sample analysis only on a case-by-case basis. Applicants may use any analytical method they consider appropriate. The analytical methods used to satisfy the requirements of this guideline will not be evaluated by the more rigorous standards concerning reproducibility, accuracy, and precision applicable to the verification methods shown in OPPTS 830.1800. Applicants should describe each method in detail and to state its precision and accuracy.

(C) Preliminary analysis of product samples may be completed prior to registration using pilot plant samples or, upon request from the registrant, may be delayed until after full scale production begins, in which case the analysis of the pilot samples for impurities should not be included with the data. All impurities present at greater than 0.1 percent and if of toxicological significance at levels of less than 0.1% should be determined for all samples.

(D) As stated in 53 FR 15952, May 4, 1988 (see paragraph (g)(5) of this guideline), the Agency has identified in two ways that impurities for which it believes that certified limits are necessary.

(1) The first is a list of specific substances or classes of substances of known toxicological concern. In some cases, the listed substances are currently or have been the subject of regulatory action against pesticide products because of the risks posed by their presence as impurities in the product. In other cases, they are identified because, historically they are known to contribute significantly to the toxic profile of an active ingredient. For example, the oxygen analogs of organophosphate pesticides may be more toxic than the parent compound and must be considered in setting tolerances for the toxicologically active components of the pesticide.

(2) The second is a set of criteria for substances which are potentially of toxicological significance; in this latter list, no specific substances are named. While substances meeting the criteria of this second list are not necessarily hazardous, nor have risks associated with their presence been quantified in any specific instance, they are typical of the types of impurities that the Agency has found to be of significance in the past.

(3) Impurities and classes of impurities of toxicological concern include but are not limited to:

(i) Hexachlorobenzene (HCB)

(ii) Ethylene thiourea (ETU)

(iii) Dichloro diphenyl trichloroethane (DDT) and other chlorinated diphenyl ethanes and ethylenes, such as analogs and isomers of DDT, DDD, DDE and Cl-DDT (“extrachloro DDT”)

(iv) Sulfotep (tetraethyl thiodiphosphate)

(v) Halogenated dibenzodioxins

(vi) Halogenated dibenzofurans

(vii) Nitrosamines

(viii) Anilines and substituted anilines

(ix) Hydrazines

(x) Oxygen analogs of organophosphates

(xi) Sulfoxides and sulfones of organophosphates and carbamates

(4) Impurities having characteristics of potential toxicological significance:

(i) Any impurity that is structurally related to a parent compound of toxicological significance.

(ii) Any impurity that is also an active ingredient.

(iii) Any impurity that is identified in standard toxicology data bases such as Toxline as being oncogenic, neurotoxic, or a developmental toxicant.

(5) This list is not exhaustive and may be expanded as new information on impurities becomes available. The Agency has reserved the right to require certified limits for other impurities on a case-by-case basis. Registrants should contact the Agency if there is a question about the status of any individual impurity not listed.

(6) These analyses, when required, should be to the lowest attainable limit of detection (this varies according to sample and chemical), but must certainly be lower than 0.1 per cent.

(vii) **OPPTS 830.1750 Certified limits.** (A) OPPTS 830.1750 requests applicants to explain how they determined the certified limits for the ingredients in their products. In addition, this section describes certain

requirements concerning certified limits and explains that certified limits are used in two ways. First, EPA reviews the composition of pesticide products to determine whether the product will cause unreasonable adverse effects on the environment. This review will involve, among other things, an evaluation of the upper bound of the toxicity of a product, that is, the toxicity of a product if the most hazardous ingredients were present in the product at the upper certified limits set for such ingredients. Second, certified limits will become the basis for future enforcement actions. FIFRA section 12(a)(1)(C) states that it is unlawful to sell or distribute:

* * *any registered pesticide the composition of which differs at the time of its distribution or sale from its composition as described in the statement required in connection with its registration under section 3.

(B) The “statement required in connection with its registration” is the statement of formula described in OPPTS 830.1550. Once a statement of formula containing certified limits has been submitted for a product, each quantity of the pesticide in commerce must conform to the composition described in the statement of formula (i.e., the amount of each ingredient must fall within the certified limits) or the product will be considered in violation of FIFRA section 12(a)(1)(C).

(C) The certified limits required for each active ingredient are intended to encompass good manufacturing practice variations (40 CFR 158.175(c)(3)). The upper and lower certified limits, which must be submitted for registration, represent the amounts of an ingredient that may legally be present (40 CFR 158.175). The lower certified limit is used as the enforceable lower limit for the product composition, while the nominal concentration appearing on the label would be the amount typically found in the product.

(D) The Agency has compliance mechanisms, such as sampling and analysis of products found in the marketplace, that are aimed at assuring that products contain amounts of active ingredients which are within the upper and lower certified limits accepted as part of the registration of those products.

(E) The guideline states that a certified limit is valid as long as the product is in commerce or until a specific expiration date stated on the label. Thus, an applicant needs to predict how long the product is likely to remain in commerce and what storage conditions may occur during that period. Based on this information and his knowledge of the chemistry of the product, the applicant then needs to establish certified limits that take into account possible degradation of the product’s ingredients. If an applicant expects the product to contain one or more ingredients that degrade rapidly, the applicant can place a specific expiration date on the label of the product and a statement that the product should not be used after that date.

(F) Applicants are requested to set, for intentionally-added ingredients and impurities, limits based on a consideration of product variability. The limits stated should not greatly exceed those actually occurring in the product when normal quality assurance procedures are used in the production process. At the same time, the stated ranges should define product composition sufficiently for the Agency to determine its suitability for registration.

(G) Also, this guideline specifies the ingredients for which certified limits are needed. For manufacturing-use products and those end-use products produced by an integrated system, the applicant must report upper and lower certified limits for active ingredients and intentionally-added inert ingredients and upper certified limits for impurities associated with an active ingredient which were found or theorized to be present in quantities equal to or greater than 0.1 percent of the product. Once again, for reasons discussed earlier, end-use products not produced by an integrated system are subject to less stringent requirements. For those products, applicants are only required to provide upper and lower certified limits for active and intentionally-added inert ingredients; upper certified limits for the impurities in those products are not routinely required. Of course, on a case-by-case basis EPA may require additional certified limits.

(H) These regulatory and enforcement efforts will continue to be used to ensure that pesticide products contain what is declared on the label.

(viii) **OPPTS 830.1800 Enforcement analytical methods.** (A) Under OPPTS 830.1800, applicants are requested to submit an analytical method for detecting and measuring the quantity of each active ingredient (and certain impurities) in their products, i.e., the TGAI, MP, or EP, depending on the product in question. The requirements for analysis of product batches apply to manufacturing-use products (including those containing solely the TGAI) and end-use products produced by an integrated system. Data on other end-use products will be required on a case-by-case basis. For pesticides in the development stage, a rudimentary product analytical method and data will suffice to support an experimental use permit. These methods must be capable of determining whether the ingredient falls within its certified limits and also must be suitable for use in state and federal enforcement programs. Therefore, the applicants must submit data to establish the precision and accuracy of these methods.

(B) Analytical methods are needed for all active ingredients and all impurities present at greater than 0.1 percent, and for toxicologically significant impurities, but not for inerts at the present time. Validation data for both accuracy and precision should be submitted for all methods. As with other requirements, the Agency may require, on a case-by-case basis, methods for additional ingredients (e.g., low level impurities or intentionally-added inerts). Analytical methods for the active ingredient may be validated by EPA laboratories at the time the product chemistry data

are reviewed. Methods should not be claimed confidential, should use commonly available equipment, and should be written to include all steps performed even when the analyst believes that certain steps are “normally” performed in all laboratories.

(ix) **OPPTS 830.1900 Submittal of samples.** (A) OPPTS 830.1900 requests that a sample of an analytically-pure grade of each active ingredient and the technical grade of each active ingredient in a product be submitted to EPA. It is usually sufficient for only one applicant to submit the analytical grade sample, and for all other applicants seeking to register a pesticide product containing that active ingredient to rely on the first applicant’s submission. However, the same approach does not work with regard to submission of technical grade chemicals. Each and every producer of a technical grade of an active ingredient (TGAI) is required to submit a sample and each applicant must specify which TGAI is used to formulate his product.

(B) The purpose of the requirement to submit samples is for EPA to have a small quantity of a known substance which EPA can then use in validating its enforcement results and in making comparisons between similar products manufactured by different producers.

(2) **Physical/chemical properties test guidelines.** (i) OPPTS guidelines 830.6302 through 830.7950 contain methods for submission of data on the physical and chemical characteristics of a pesticide product and its ingredients, particularly the active ingredient. These data requirements are subject to the formulators’ exemption contained in FIFRA section 3(c)(2)(D). These requirements have a variety of purposes. Some characteristics, such as explosiveness and flammability, are directly related to hazards to humans. EPA requires data on other characteristics, e.g., solubility and viscosity, to assess the behavior of the product when it is used. Still other properties like color, density, and odor are used to identify the pesticide in emergency situations. Some characteristics, such as melting and boiling points, are relevant to the review and evaluation of the manufacturing process.

(ii) The Agency requires applicants to add warning statements to their product labels on the basis of these physical and chemical characteristics. EPA may also require changes in use directions based on physical and chemical characteristics of the products.

(iii) For the most part, the physical and chemical characteristics covered by these guidelines are determined routinely for all pesticide products. Moreover, these characteristics are usually determined with testing techniques which were standardized years ago and are now widely used. Each of these guidelines contains a reference paragraph which cites standardized testing techniques, including those published by the Organization for Economic Cooperation and Development (OECD), the American Society for

Testing and Materials (ASTM), or the Collaborative International Pesticide Analytical Council, Limited (CIPAC). While EPA recommends that these protocols be used where appropriate, the Agency will accept determinations made using other techniques, so long as the techniques are validated and the specific test standards in the appropriate guidelines are satisfied. It is recommended that the applicant contact the Agency to discuss alternative methods prior to their use.

(iv) Certain specific considerations apply to the development of physical/chemical data for pesticides. These are summarized in the following paragraphs.

(v) Good Laboratory Practice (GLP) Requirements. (A) All provisions of the GLP standards, including those listed in 40 CFR 160.135 (a) and (b) apply to the following studies:

Old guideline number	New guideline number	Title
62-1	830.1700	Preliminary Analysis
63-8*	830.7840	Water Solubility
	830.7860	
63-9*	830.7950	Vapor Pressure
63-11*	830.7550	Octanol/water Partition Coefficient
	830.7560	
	830.7570	
63-13*	830.6313	Stability to Normal and Elevated Temperatures, Metals, and Metal Ions
63-17	830.6317	Storage Stability

* For items marked with an asterisk, certification for GLP standards is required only for technical products (TGAI), not for end-use products (EP) unless these end-use products are produced by an integrated system.

(B) The provisions of the GLP standards also apply to the studies listed below. However, for the listed studies, not all GLP provisions are applicable. The standards which do not apply are specified in 40 CFR 160.135 and registrants and laboratories conducting the studies should consult 40 CFR part 160 for further details.

Old guideline number	New guideline number	Title
63-2	830.6302	Color
63-3	830.6303	Physical State
63-4	830.6304	Odor
63-5*	830.7200	Melting Point
63-6*	830.7220	Boiling Point
63-7	830.7300	Density/Relative Density/Bulk Density
63-10*	830.7370	Dissociation Constant
63-12	830.7000	pH
63-14	830.6314	Oxidizing or Reducing Action: Chemical Incompatibility
63-15	830.6315	Flammability
63-16	830.6316	Explosibility
63-18	830.7100	Viscosity
63-19	830.6319	Miscibility
63-20	830.6320	Corrosion Characteristics
63-21	830.6321	Dielectric Breakdown Voltage
None	830.7050	UV/Visible absorption

* For items marked with an asterisk, certification for GLP standards is required only for technical products (TGAI), not for end-use products (EP) unless these end-use products are produced by an integrated system.

(C) Registrants are also reminded that the GLP certification statement required by Pesticide Regulation Notice PR 86-5 (see paragraph (g)(2) of this guideline) must be signed by both the sponsor and the study director.

(vi) **OPPTS 830.6302 (Color) and 830.6304 (Odor).** (TGAI, MP). Under 40 CFR 158.190, data on color and odor are required for TGAI and MP forms of the pesticide. In Pesticide Regulation Notice PR 92-5 (see paragraph (g)(4) of this guideline), the Agency waived the requirement that data for color and odor be generated or submitted for EP products because EPA has approved alternate formulations containing substitute colorants and odorants. This waiver does not apply when color and/or odor are expected to affect product performance (efficacy). In those cases, the Agency reserves the right to request the submission of such data from applicants or registrants in order to make required statutory findings. The Agency reserves the right to require the generation and submission of color and odor data any time it determines that such data are needed to make required statutory findings.

(vii) **OPPTS 830.6315 Flammability.** (MP, EP). The flash point determination should be conducted on the entire formulated product, not on the active ingredient per se. For aerosols, the flame extension test method should be conducted.

(viii) **OPPTS 830.6317 Storage stability.** (MP, EP). Data on storage stability is required for the MP form of the pesticide. The requirement for data on the EP applies only when: The product use pattern is one for which performance (efficacy) data are required (40 CFR 158.640); the results of the storage stability study indicate that the concentration of any active ingredient is not within the certified limits or degradates of toxicological significance are detected in the study; or product instability is suspected or incidents of instability are reported. Previously, under Pesticide Regulation Notice PR 92-5 (see paragraph (g)(4) of this guideline), this requirement for EP data submittal was waived until the Agency could develop alternative test methodologies which would permit the evaluation of pesticide product composition for lengths of time in excess of one year. The newly developed guideline permits extension of testing for longer than one year if the product is expected to be on the market for longer than one year or expected to be efficacious for longer than one year.

(ix) **OPPTS 830.6320 Corrosion characteristics.** (MP, EP). Data not required if explanation of lack of corrosivity is reasonable (e.g., lack of extreme pH, lack of reaction with container material).

(x) **OPPTS 830.7840 and 830.7860 Solubility.** (TGAI). In addition to the water solubility data requirements of OPPTS 830.7840 and 830.7860, solvents should include n-octanol and representative polar and non-polar solvents (e.g., methanol and hexane) commonly used for pesticides. Several commonly accepted test methods for organic solubility are available and registrants should discuss the choice of methods with the Registration Division prior to conducting the test.

(xi) **General.** (A) Several test methods call for the use of distilled water. Although double distilled water is preferred, deionized water with a resistivity above 10 megohms/cm and a total organic content below 0.01 per cent can also be used. Therefore, any water purification system can be used provided that these required quality criteria are met.

(B) The following Table 2 summarizes the substance to be tested in each guideline study. Circumstances when the test is required are encoded in 40 CFR part 158.

Table 2.—Summary of Substances to be Tested in Each 830 Series Guideline

New guideline	1982 guideline	Title	Test substance		
			Technical grade of active ingredients	Manufacturing-use product	End-use product
830.1550	158.155	Product identity and composition	Yes ¹	Yes ¹	Yes ¹
830.1600	158.160	Description of Materials used to produce the product	Yes ¹	Yes ¹	Yes ¹
830.1620	158.162	Description of production process	Yes ¹	Yes ¹	Yes ¹
830.1650	158.165	Description of formulation process	Yes ¹	Yes ¹	Yes ¹
830.1670	158.167	Discussion of formation of impurities	Yes ¹	Yes ¹	Yes ¹
830.1700	158.170	Preliminary analysis	Yes ¹	Yes ¹	Yes ¹
830.1750	158.175	Certified limits	Yes ¹	Yes ¹	Yes ¹
830.1800	158.180	Enforcement analytical method	Yes ¹	Yes ¹	Yes ¹
830.1900	64-1	Submittal of samples	Yes	Case-by-case	Case-by-case
830.6302	63-2	Color	Yes	Yes	No
830.6303	63-3	Physical state	Yes	Yes	Yes
830.6304	63-4	Odor	Yes	Yes	No
830.6313	63-13	Stability to normal and elevated temperatures, metals, and metal ions	Yes	No	No
830.6314	63-14	Oxidation/reduction: chemical incompatibility	No	Yes	Yes
830.6315	63-15	Flammability	No	Yes	Yes
830.6316	63-16	Explosibility	No	Yes	Yes
830.6317	63-17	Storage stability	No	Yes	Yes
830.6319	63-19	Miscibility	No	Yes	Yes
830.6320	63-20	Corrosion characteristics	No	Yes	Yes
830.6321	63-21	Dielectric breakdown voltage	No	No	Yes
830.7000	63-12	pH	Yes	Yes	Yes
830.7050	None	UV/visible absorption	Yes (PAI)	No	No
830.7100	63-18	Viscosity	No	Yes	Yes
830.7200	63-5	Melting point/melting range	Yes (solids—PAI)	No	No
830.7220	63-6	Boiling point/boiling range	Yes (liquids—PAI)	No	No
830.7300	63-7	Density/relative density/bulk density	Yes	Yes	Yes
830.7370	63-10	Dissociation constant	Case-by-case (PAI)	No	No
830.7550	63-11	Petition coefficient (<i>n</i> -octanol/water), shake flask method	Yes (for non-polar organics—PAI)	No	No
830.7560	63-11	Petition coefficient (<i>n</i> -octanol/water), generator column method	Yes (for non-polar organics—PAI)	No	No
830.7570	63-11	Petition coefficient (<i>n</i> -octanol/water), estimation by liquid chromatography	Yes (for non-polar organics—PAI)	No	No
830.7840	63-8	Water solubility: Column elution method; shake flask method	Yes (PAI)	No	No
830.7860	63-8	Water solubility, generator column method	Yes (PAI)	No	No
830.7950	63-9	Vapor pressure	Yes (PAI)	No	No

¹ Requirements pertaining to Product Identity, Composition, and Analysis are detailed further in the respective Test Guidelines OPPTS 830.1550 through 830.1800.

(f) **Data reporting—(1) Data reporting guidance.** Data submitters are encouraged to produce complete reports for efficient review by the Agency. This section pertains to organizing and presenting the substance of the data report. Pesticide Regulation Notice PR 86-5 (see paragraph (g)(2) of this guideline) pertains to physical formatting of reports (which are referred to as “studies”) and submittal packages.

(2) **Data reporting format.** The following paragraphs describe the general order and format for submittal of data requirements for product

chemistry. (Additional data requirements may be required as specified in the individual test guidelines.)

(i) *Title/cover page.* Title page and additional documentation requirements (i.e., requirements for data submission and statements of data confidentiality claims), if relevant to the study report, should precede the content of the study formatted below. These requirements are described in PR Notice 86–5 (see paragraph (g)(2) of this guideline).

(ii) *Table of contents.*

(A) *Introduction and summary.* (1) *Scope*—procedure/tests used (including sources).

(2) Principles of the procedure/test used including any references which may be applicable.

(B) *Materials and methods.* (1) *Equipment*—(list and describe).

(2) Reagents and standards (if applicable)—list and describe source and preparation.

(3) *Procedures*—detailed stepwise description of procedure employed in test.

(4) *Instrumentation*—detailed description of equipment employed in test.

(5) *Methods of calculation* (if applicable).

(6) *Other*—any and all additional information that the registrant considers appropriate and relevant.

(C) *Conclusions.* Discussion of the adequacy of procedures or tests as well as whether the results provide acceptable accuracy and precision. Discuss any other points which may have a bearing on the information/data provided.

(D) *Certification.* Certification of authenticity by the sponsor and the study director (including signature, typed name, title, affiliations, address, telephone number, and date).

(E) *Tables and figures* (where appropriate).

(F) *References.*

(G) *Appendices.* Include: Representative chromatograms, etc., or any other relevant material not fitting in any of the other sections of the report.

(3) **Submittal package organization.** As specified in PR notice 86–5 (see paragraph (g)(2) of this guideline), submittal packages should be

organized in the following manner. (Additional details are provided in PR Notice 86–5).

(i) All product chemistry data within a submittal package submitted in support of an end-use product produced from registered manufacturing-use products should be bound as a single study under a single title page.

(ii) Product chemistry data submitted in support of a technical product, other manufacturing-use product, an experimental use permit, an import tolerance petition, or an end-use product produced from unregistered source ingredients, should be bound as a single study for each guideline group: Group A—Product identity, composition, and analysis (830.1550 through 830.1800) and Group B—Physical/ chemical properties (830.6302 through 830.7950).

(4) **The formulators’ exemption.** (i) FIFRA section 3(c)(2)(D) provides that:

* * * No applicant for registration of a pesticide who proposes to purchase a registered pesticide from another producer in order to formulate such purchased pesticide into an end-use product shall be required to

(i) submit or cite data pertaining to the safety of such purchased product; or

(ii) offer to pay reasonable compensation otherwise required by FIFRA section 3(c)(1)(D) for the use of any such data.

(ii) This section, commonly called the “formulators’ exemption” or the “horizontal line provision,” relieves formulators of end-use products from the obligation to provide data concerning the safety of ingredients in registered pesticide products they purchase.

(iii) The formulators’ exemption applies primarily to the physical and chemical characteristics portion of the product chemistry guidelines (OPPTS 830.6302 through 830.7950). Certain sections of that portion of the guidelines require data on the technical chemical to support the registration of both end-use products and manufacturing-use products. If an end-use product is manufactured by using a purchased, registered manufacturing-use product, the end-use product registrant is exempted by FIFRA section 3(c)(2)(D) from submitting physical and chemical property data on the active ingredient(s) in the manufacturing-use products. Similarly, if an applicant uses a purchased, registered end-use product to produce his own end-use product, and the label of the applicant’s product contains only uses which appear on the label of the purchased product, the applicant is covered by the formulators’ exemption. The primary result of the formulators’ exemption is to lessen the data requirements for companies that simply use a registered pesticide to make their end-use products.

(g) **References.** The following references should be consulted for additional background material on this test guideline.

(1) Environmental Protection Agency, Pesticide Assessment Guidelines, Subdivision D: Product Chemistry, Series 61-4, Addendum 1 on Data Reporting, 1988, EPA Report 540/09-88-048.

(2) Environmental Protection Agency, Pesticide Registration Notice PR 86-5, Standard Format for Data Submitted under FIFRA and Certain Provisions of the FFDCA, July 29, 1986.

(3) Environmental Protection Agency, Office of Pesticide Programs, Registration Division, Memorandum titled "Roadmap for Guidance to Product Chemistry Guidelines," dated November 20, 1989.

(4) Environmental Protection Agency, Pesticide Regulation Notice PR 92-5, "Product Chemistry Data Requirements for Registration and Reregistration of End-Use Products," October 9, 1992.

(5) FEDERAL REGISTER 53:15952, May 4, 1988, Final Rule, Pesticide Registration Procedures; Pesticide Data Requirements.