ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 152 and 158

[OPP–2004–0387; FRL–6811–2]

RIN 2070–AC12

Pesticides; Data Requirement for Conventional Chemicals

AGENCY: Environmental Protection Agency (EPA).

ACTION: Proposed rule.

SUMMARY: EPA proposes to update and revise its data requirements for the registration of conventional pesticide products. These data requirements and those already codified in part 158 of title 40 of the Code of Federal Regulations (CFR), are intended to provide EPA with data and other information necessary for the registration of a conventional pesticide chemical. Since the data requirements in part 158 were first codified in 1984, information needed to support the registration of a pesticide chemical has evolved as the general scientific understanding of the potential hazards posed by pesticides has grown. Over the years, updated data requirements were developed by EPA using a process that involved public participation and extensive involvement by the scientific community, including peer review by the FIFRA Scientific Advisory Panel (SAP). Most of the data requirements contained in this proposal have been applied on a case-by-case basis to support individual applications, or imposed via Data Call-In (DCI) on all registrants of similar products. Although the data requirements imposed have progressed as scientific understanding and concerns have evolved, the codified data requirements have not been updated to keep pace. This proposal involves changes to the codified data requirements that pertain to product chemistry, toxicology, residue chemistry, applicator exposure, post-application exposure, nontarget terrestrial and aquatic organisms, nontarget plant protection, and environmental fate. Coupled with updating data requirements, EPA proposes to add a few new studies, reformat the requirements, and revise its general procedures and policies associated with data submission. By codifying existing data requirements which are currently applied on a case-by-case basis, the pesticide industry, along with other partners in the regulated community, attain a better understanding and are better prepared for the pesticide registration process. This proposed rule does not apply to the data requirements for the registration of antimicrobial pesticide products; inert ingredients for pesticide products; spray drift, product performance (efficacy); or biochemical, and microbial pesticides.

DATES: Comments must be received on or before June 9, 2005.

ADDRESSES: Submit your comments, identified by Docket ID No. OPP–2004–0387, by one of the following methods:

- *Federal eRulemaking Portal. http://www.regulations.gov.* Follow the on-line instructions for submitting comments.
- *Agency Web Site. http://www.epa.gov/edocket.* EDOCKET, EPA's electronic public docket and comment system, is EPA's preferred method for receiving comments. Follow the on-line instructions for submitting comments.
- *E-mail. opp-docket@epa.gov*.
- *Mail*. Public Information and Records Integrity Branch (PIRIB) (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460–0001.
- *Hand Delivery*. Public Information and Records Integrity Branch (PIRIB), Office of Pesticide Programs (OPP), Environmental Protection Agency, Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA. Such deliveries are only accepted during the Docket's normal hours of operation, and special arrangements should be made for deliveries of boxed information.

Instructions. Direct your comments to Docket ID No. OPP–2004–0387. EPA's policy is that all comments received will be included in the public docket without change and may be made available online at *http://www.epa.gov/edocket*, including any personal information provided, unless the comment includes information claimed to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through EDOCKET, regulations.gov, or e-mail. The EPA EDOCKET and the federal regulations.gov websites are ''anonymous access '' systems, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through EDOCKET or regulations.gov, your e-mail address will be automatically captured and included as part of the comment that is placed in the public docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any disk or CD-ROM you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses. For additional information about EPA's public docket visit EDOCKET on-line or see the **Federal Register** of May 31, 2002 (67 FR 38102). For additional instructions on submitting comments, go to Unit I.B. of the **SUPPLEMENTARY INFORMATION** section of this document.

Docket. All documents in the docket are listed in the EDOCKET index at *http://www.epa.gov/edocket.* Although listed in the index, some information is not publicly available, *i.e.*, CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, is not placed on the Internet and will be publicly available only in hard copy form. Publicly available docket materials are available either electronically in EDOCKET or in hard copy at the Public Information and Records Integrity Branch (PIRIB), Rm. 119, Crystal Mall #2, 1801 S. Bell St., Arlington, VA. This docket facility is open from 8:30 a.m. to 4 p.m., Monday through Friday, excluding legal holidays. The docket telephone number is (703) 305–5805.

FOR FURTHER INFORMATION CONTACT: Vera Au, Field and External Affairs Division (FEAD), Office of Pesticide Programs, Mailcode: 7506C, Environmental Protection Agency, 1200 Pennsylvania Ave. NW., Washington, DC 20460; telephone number: (703) 308–9069: fax number: 703–305–5884; e-mail address: *au.vera@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be affected by this action if you are a producer or registrant of a pesticide product, including agricultural, residential, and industrial pesticides, but not including antimicrobial, biochemical or microbial pesticides, or inert ingredients in pesticide products. This proposal also may affect any person or company who might petition the Agency for new tolerances, hold a pesticide registration with existing tolerances, or any person or company who is interested in obtaining or retaining a tolerance in the absence of a registration, that is, an import tolerance. This latter group may

include pesticide manufacturers or formulators, importers of food, grower groups, or any person or company who seeks a tolerance. Potentially affected entities may include, but are not limited to:

Chemical Producers (NAICS 32532), *e.g.*, pesticide manufacturers or formulators of pesticide products, importers or any person or company who seeks to register a pesticide or to obtain a tolerance for a pesticide.

This listing is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be affected by this action. Other types of entities not listed above could also be affected. The North American Industrial Classification System (NAICS) codes have been provided to assist you and others in determining whether this action might apply to certain entities. If you have any questions regarding the applicability of this action to a particular entity, please consult the appropriate Branch Chief in the Registration Division of the Office of Pesticide Programs at 703–305–5447.

B. What Should I Consider as I Prepare My Comments for EPA?

1. *Submitting CBI.* Do not submit this information to EPA through EDOCKET, regulations.gov or e-mail. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD ROM that you mail to EPA, mark the outside of the disk or CD ROM as CBI and then identify electronically within the disk or CD ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for Preparing Your Comments.* When submitting comments, remember to:

- Identify the rulemaking by docket number and other identifying information (subject heading, **Federal Register** date and page number).
- Follow directions - The agency may ask you to respond to specific questions or organize comments by referencing a Code of Federal Regulations (CFR) part or section number.
- Explain why you agree or disagree; suggest alternatives and substitute language for your requested changes.
- Describe any assumptions and provide any technical information and/or data that you used.
- If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.
- Provide specific examples to illustrate your concerns, and suggest alternatives.
- Explain your views as clearly as possible, avoiding the use of profanity or personal threats.
- Make sure to submit your comments by the comment period deadline identified.

II. Organization of Preamble

This preamble is organized according to the outline in this unit.

III. Statutory Authorities and Regulatory Framework

EPA is authorized to regulate pesticides under two federal statutes. The Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) regulates the sale, distribution, and use of pesticide products through a licensing (registration) scheme. The Federal Food, Drug and Cosmetic Act (FFDCA), among other things, regulates the safety of pesticide residues in food and feed. Both FIFRA and FFDCA were amended in 1996 by the Food Quality Protection Act (FQPA) to strengthen the protections offered, with particular emphasis on protection of children.

This action is issued under the authority of secs. 3, 4, 5, 10, 12, and 25 of FIFRA (7 U.S.C. 136–136y) and sec. 408 of FFDCA (21 U.S.C. 346a). The data required for a registration, reregistration, experimental use permit, or tolerance are listed in 40 CFR part 158.

A. FIFRA

Under FIFRA, every pesticide product must be registered (or specifically exempted from registration under FIFRA sec. 25(b)) with EPA before it may be sold or distributed in the United States. To obtain a registration, an applicant or registrant must demonstrate to the Agency's satisfaction that, among other things, the pesticide product, when used in accordance with widespread and commonly recognized practice, will not cause ''unreasonable adverse effects'' to humans or the environment. This safety determination, as defined in the statute, requires the Agency to consider the risk of the use of the pesticide and weigh this against its benefit. EPA must determine that the safety standard contained in FIFRA is met before granting a federal pesticide registration.

1. *Registration.* Section 3 of FIFRA contains the requirements for registration. Specifically, FIFRA sec. 3(c)(2) provides EPA broad authority, before and after registration, to require scientific testing and submission of the resulting data to the Agency by registrants and applicants of pesticide products. An applicant for registration must furnish EPA with substantial amounts of data on the pesticide, its composition, toxicity, potential human exposure, environmental properties and ecological effects, as well as information on its efficacy in certain cases. Although the data requirements are imposed primarily as a part of initial registration, EPA is authorized under FIFRA sec. 3(c)(2)(B) to require a registrant to develop and submit additional data to maintain a registration. This post registration data call-in authority recognizes that the scientific underpinnings of risk assessment change, and is another means by which EPA may keep data for use in risk assessment current with evolving science.

2. *Reregistration.* FIFRA sec. 4 requires that EPA reregister each pesticide product first registered before November 1984. This date was chosen based upon the fact that pesticides registered since 1984 were subject to the part 158 requirements of the 1984 regulation. Additional data for older

pesticides were called in where gaps in the scientific data base occurred. The Agency has largely used its data call-in authority to require on a case-by-case basis the submission of most of the data requirements contained in this proposal.

3. *Experimental use permits.* Subject to some exceptions, FIFRA sec. 5 requires persons seeking experimental use of pesticides under field conditions to obtain an experimental use permit (EUP). An EUP allows limited use of a pesticide for specified experimental and data collection purposes intended to support future registration of the pesticide. Because an EUP is for limited use under controlled conditions, the data needed to support issuance of the permit are correspondingly less than those required for full registration. For example, when performing crop field trials, a registrant may opt to destroy the treated crop rather than generate the needed residue chemistry data to establish a temporary tolerance. The regulations governing the issuance of EUPs are found in 40 CFR part 172.

B. FFDCA

FFDCA mandates EPA to determine that the level of pesticide chemical residues in food and feed will be safe for human consumption. An applicant must petition the Agency for a tolerance (maximum residue level) for a pesticide that is to be used in or around food or feed commodities, or could otherwise come in contact with food or feed. The safety standard set under FFDCA sec. 408(b) and (c) defines safe as ''a reasonable certainty that no harm '' will result from exposures to pesticide chemical residues. In making this determination, EPA is directed to consider aggregate risks from multiple sources of pesticide exposure, including anticipated food, drinking water, and other non-occupational exposures for which there is reliable information. Under FFDCA sec. 408(b)(2)(C), EPA must make a separate finding of safety for infants and children. In addition, EPA must take into account a variety of other factors, enumerated in sec. 408(b)(2)(D), including the cumulative risks associated with pesticides having a common mechanism of toxicity. The combination of aggregate and cumulative exposure increases the nature and scope of EPA's risk assessment, and potentially the types and amounts of data needed to determine that the FFDCA safety standard is met.

1. *Establishing tolerances.* Under FFDCA sec. 408, EPA is authorized to establish tolerances for pesticide residues in food and feed, or to exempt a pesticide from the requirement of a tolerance, if warranted. In this preamble, references to tolerances include exemptions from tolerance since the standards and procedures for both are the same. As previously mentioned, in 1996, FQPA modified FFDCA to establish a single health-based standard for tolerance-setting and enhanced the risk assessment process to more clearly focus on pesticide risks to children. The new safety standard applies to tolerances in a number of regulatory situations, including:

- Permanent tolerances that support registration under FIFRA;
- Tolerances for imported products which are established to allow importation of pesticide-treated commodities, but for which no U.S. registration is sought;
- Time-limited tolerances which are established for FIFRA sec. 18 emergency exemptions; and
- Temporary tolerances established for experimental use permits under FIFRA sec. 5.

2. *Reassessing tolerances.* Under FFDCA sec. 408(q), EPA must reassess each tolerance established before August 3, 1996, on a prescribed 10–year schedule. The Agency has reassessed many tolerances under its reregistration program. Numerous regulatory decisions have been made based upon available data and information required by the existing data requirements, and supplemented by additional data provided by registrants through data call-ins or voluntary submissions.

C. Linking FIFRA and FFDCA Safety Standards

Unless EPA is able to establish or maintain a needed tolerance or exemption under FFDCA, a pesticide cannot be registered under FIFRA for a food/feed use. FQPA created a specific linkage (FIFRA sec. 2(bb)) between the ''unreasonable adverse effects'' finding under FIFRA and the determination of pesticide residue safety of ''reasonable certainty of no harm'' under FFDCA. In essence, a pesticide that is inconsistent with, or does not meet, the FFDCA sec. 408 safety standard poses an unreasonable adverse effect that precludes new or continued registration. Thus, both FIFRA and FFDCA standards must be met for pesticides intended to be registered in the United States for food or feed uses.

Given this linkage between registration and tolerances, it makes sense for EPA to define data requirements for both purposes: the data required to support a determination of ''reasonable certainty of no harm'' under FFDCA are an integral part of the data needed for an ''unreasonable adverse effects'' determination under FIFRA. Consequently, when promulgated, these proposed data requirements would encompass the basic data requirements for both registration and tolerance-setting determinations. EPA will retain its authority to require additional data on a case-by-case basis.

IV. Background

A. Why does EPA Require Data for Pesticide Registrations?

Under the FFDCA and the FIFRA, anyone seeking to register a pesticide product is required to provide information to EPA that demonstrates their products can be used without posing unreasonable risk to human health and the environment, and for food uses, that there is a reasonable certainty that no harm will result from exposures to the residues of their pesticide product. As appropriate for the particular pesticide product, EPA uses the information provided to evaluate the pesticide for a wide range of adverse human health effects, from eye and skin irritation to cancer and birth defects, and to assess how the pesticide affects animal and plant species, non-target insect species, and what happens to the pesticide in soil, water, and air.

B. What are the Data Requirements?

First promulgated in 1984, the data requirements in 40 CFR part 158 outline the kinds of data and related information typically needed to register a pesticide. The data requirements are organized by major pesticide type (*e.g.*, conventional, antimicrobial, biochemical/microbial, etc.), scientific discipline (*e.g.*, toxicology, etc.), and major use site (*e.g.*, outdoor vs. indoor). Part 158 also outlines the associated procedures for submitting the data, requesting a waiver from a requirements, and other associated procedures. Since there is much variety in pesticide chemistry, exposure, and hazard, part 158 is designed to be flexible. Table notes to each data requirement explain under what conditions data are typically needed. The Agency also recognizes, however, that due to the particular nature and risk of some pesticides, registrants may seek to obtain data waivers or may suggest alternative approaches to satisfying requirements. Over the years since 1984, other data requirements have been implemented on a case-by-case basis. The determination of what data or information is needed is based on a scientifically rigorous process that includes peer review by the FIFRA Scientific Advisory Panel (SAP), as well

as a public review and comment process.

In essence, the data requirements identify the questions that the registrant will need to answer regarding the safety of a pesticide product before the Agency can register it. The data requirements address both components of a risk assessment, *i.e.*, what hazards does the pesticide present, and what level of exposure. The answer to one question may inform the kind of information needed in others. For example, a pesticide that is persistent and toxicologically potent may require more extensive exposure data to help establish a safe level of exposure. If there is negligible exposure then there may be generally less need for extensive hazard data since any conceivable risk would be low.

1. *The establishment of standardized data requirements.* Until 1984, data requirements were based on longstanding requirements initially put in place when pesticides were regulated by the U.S. Department of Agriculture (USDA) and the Food and Drug Administration (FDA). However, because virtually all of EPA's decisions relating to the registration of pesticides or the establishment of tolerances depend on Agency evaluation of scientific studies, EPA has throughout the years developed standardized data requirements and test guidelines, and established evaluation procedures and peer review processes to ensure the quality and consistency of scientific studies.

The current provisions in part 158 were originally promulgated in October, 1984. Prior to this, data requirements for the registration of pesticides were contained in a variety of guidance documents, not in regulatory form. Part 158 was intended to be a concise presentation of what data were required and under what circumstances. Once codified, part 158 specified standard hazard and exposure studies required for registration and tolerance setting and also identified conditions under which more specialized studies might be required. Guidelines, *i.e.*, instructions and test methods on how to perform a study, had meanwhile been issued as a series of Pesticide Assessment Guidelines. These documents, updated in 1996, describe acceptable protocols, test conditions, and data reporting guidelines to ensure that EPA's regulatory decisions are based on sound scientific data.

2. *Relationship between the harmonized test guidelines and part 158 requirements.* EPA has established a unified library for test guidelines issued by the Office of Prevention, Pesticides and Toxic Substances (OPPTS) for use in testing chemical substances to develop data for submission to EPA under the Toxic Substances Control Act (TSCA), FFDCA or FIFRA. This unified library of test guidelines represents an Agency effort that began in 1991 to harmonize the test guidelines within OPPTS, as well as to harmonize the OPPTS test guidelines with those of the Organization for Economic Cooperation and Development (OECD) of the European Community. The process for developing and amending these test guidelines includes several opportunities for public participation and the extensive involvement of the scientific community, including peer review by the FIFRA SAP and the Science Advisory Board (SAB) and other expert scientific organizations.

The purpose for 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 Agency's data requirements under FIFRA and TSCA. The guidelines themselves do not impose mandatory requirements. Instead, they present recognized standards for conducting acceptable tests, guidance on evaluating and reporting data, definition of terms, and suggested study protocols. As such, pesticide registrants may use a non-guideline protocol to generate the data required by part 158. Typically the registrant will use the available guideline, in which case the study protocol would simply cite the relevant guideline. If the registrant deviates from these guidelines, or is asked to provide data where there isn't yet a final guideline available, the registrant will discuss the variation with EPA and will explain and justify the methods chosen in the study protocol. Non-guideline protocols are accepted, provided that the study protocol meets the purpose of the test standards specified in the guidelines, and provides data of suitable quality and completeness as typified by the protocols cited in the guidelines. More information about the unified library and these guidelines is available at *http://www.epa.gov/opptsfrs/home/guidelin.htm*.

C. Why Have the Data Needs Changed Since 1984?

1. *1988 FIFRA amendments.* In 1988, FIFRA was amended to ensure that older pesticides met the scientific standards of the day. Among other things, the amendments provided for the acceleration of the reregistration program by establishing statutory deadlines and new procedures. The 1988 changes to FIFRA are important because it was during this effort that EPA recognized that some of the 1984 data requirements were becoming out of date. The Agency then used the reregistration process to focus on needed changes.

2. *The National Academy of Sciences 1993 Report.* With increasing emphasis on protecting children's health, EPA began to examine its data requirements relative to evaluating the potential risks from pesticides to sensitive subpopulations. The Agency sought the advice of the National Academy of Sciences' National Research Council (NRC) to assess its risk assessment methodologies and to provide additional information on the extent to which children may be at risk given emerging scientific information and technologies. In their 1993 report entitled, ''Pesticides in the Diets of Infants and Children,'' (Ref. 1) NRC offered recommendations for further protecting infants and children from pesticides in their diet. The NRC called for the Agency to require more data and adopt better risk assessment methodologies. For example, the Council called for increased testing in the area of immune function, neurodevelopmental and reproductive testing, and neurotoxicity testing. NRC also suggested adding a thyroid screen to existing subchronic and chronic toxicity tests and additional tests on age-related physiological changes and pharmacokinetics in immature animals.

At the time the 1993 report was released, EPA had already begun work on many of the recommendations to improve the quality of its risk assessments. New testing guidelines and protocols were developed. Since then, many of the testing requirements recommended by the NRC have been incorporated into the Agency's standard evaluation requirements and practices. In addition, in line with the Council's recommendations and the FIFRA Scientific Advisory Panel's (SAP) advice, EPA recently expanded its neurotoxicity and developmental neurotoxicity study requirements. These updated requirements are contained in this proposal.

3. *The Food Quality Protection Act of 1996 (FQPA).* Passage of FQPA in 1996 reformed our nation's pesticide and food safety laws, resulting in changes in EPA's approach to protecting human health from risks associated with pesticide use. As mentioned, FQPA modified both FIFRA and FFDCA and established a single health-based standard for food-use pesticides and added protections for infants and children.

Throughout the 1990s, EPA has been continually working on improving data requirements. Under FFDCA, as amended by FQPA, EPA must reassess all existing pesticide tolerances and exemptions against the expanded and more rigorous safety standard. Beginning in 1994, and increasingly since the enactment of FQPA, EPA has changed aspects of its data requirements and risk assessment process to improve its ability to assess exposure more accurately and to strengthen its understanding of the potential pesticide risk to children. As mentioned, risk assessments must now consider data relating to aggregate exposure (exposure to pesticides from food, drinking water, and non-occupational routes such as home and garden uses) and cumulative risk (effects from exposures to multiple pesticides that share a common mechanism of toxicity). These measures necessitate collection of additional data on drinking water and non-occupational and residential exposure.

V. Purpose and Scope of this Proposal

A. What is the Scope of this Proposal?

This proposal applies only to conventional pesticides. In general, a conventional pesticide is considered as a synthetic chemical or a natural substance with a toxic mode of action. It is applicable to both manufacturing-use and end-use products. It does not include data requirements for antimicrobial, biochemical or microbial pesticides; inert ingredients; or changes to existing spray drift or product performance (efficacy) data requirements for conventional chemicals.

B. Why is EPA Proposing these Revisions?

EPA has a number of objectives in proposing this regulation to update and revise the data requirements in 40 CFR part 158. First, this proposal will update the requirements in part 158 to reflect changes that have occurred over time and which are generally applied already.

Second, this proposal will provide clarity on the data requirements themselves, with data requirements reformatted to promote efficiency in registration decision processes. Third, information developed in fulfilling these data requirements will improve the scientific basis supporting increasingly complex risk management decisions.

1. *Updating the 1984 requirements.* Although most of the specific requirements in part 158 have not changed since the data requirements were first published in 1984, there is information that is out-of date or may be unclear. The underlying science has advanced (*e.g.*, NAS in 1993 suggested changes to better protect children). The Agency's legislative mandate has been broadened to address new concerns. For example, given the stricter mandates imposed by the 1988 FIFRA amendments (emphasis on exposure to population subgroups) and the 1996 FQPA amendments to FIFRA and FFDCA, EPA finds that it is more frequently requesting certain data, and the Agency believes it should detail more specifically the conditions under which these tests will be required. Thus the proposed change entails both new tests and broadened requirements for some current tests.

This regulation will reflect the changes in data requirement practices that have evolved through practice since the 1984 data requirement rule was promulgated and address data needed to meet requirements created by statutory amendments to FIFRA and FFDCA. In addition, the rule will eliminate redundant data submission requirements.

EPA's underlying principle in development of this regulation is to strike an appropriate balance between the need for adequate data to make informed risk management decisions while minimizing the data collection burden.

Until this proposal is promulgated, the Agency will continue to use existing authority in 40 CFR part 158, to obtain these data on a case-by-case basis should they be necessary to support a registration.

2. *Reorganizing part 158 to improve usability.* EPA proposes to reorganize and reformat part 158 subpart A (General Provisions), and subpart B (How to Use Data Tables), and reorganize and renumber subpart D (Data Requirement Tables) into several individual subparts (see Table 1 in Unit VI). Each subpart would contain the data requirement tables for an individual scientific discipline and references to correlate with the Pesticide Assessment Guidelines. The Agency also proposes to remove from the regulations the current Appendix A, (a compendium of pesticide use sites and use categories), and create a separate Pesticide Use Index Guidance Document. Since the information contained in Appendix A only serves as reference material and is not being stated as a requirement, EPA believes that a guidance document format is easier to keep current and therefore better serves the regulated community. The information will be placed on EPA's website and made available to the public.

3. *Improving the scientific basis for pesticide registration decisions.* In general, the information developed as a result of the revisions, if finalized as proposed today, is expected to increase scientific understanding of the health and environmental effects of pesticides to which individuals and the environment may be exposed. The revised requirements are expected to improve the scientific basis for the Agency's regulatory decisions about the human health and environmental risks of pesticide products. The improved scientific basis is also expected to benefit a wide range of parties, including consumers and the general public, workers, scientists, industry, governments, public health officials, and the medical community, as well as foreign parties. Discussed in more detail in the document entitled ''Economic Analysis of the Proposed Change in Data Requirements Rule for Conventional Pesticides,'' which is available in the public docket for this rulemaking, the following briefly highlights the various ways the improved data is expected to be used:

i. *Better informed regulatory decisions allow preservation of important pesticide uses.* The proposed revisions enable the Agency to make better informed regulatory decisions based on more complete data about the potential risks of pesticides. For example, the proposed changes better target needed data that take into account human and wildlife toxicological end points or routes of exposure not now adequately covered. The proposed rule would also require better information about the potential for pesticides to cause immunotoxic or developmental neurotoxic effects. This information is expected to be valuable in assuring that pesticide residues in food or from other sources are safe for children as well as other consumers. These studies would allow the Agency to assess aggregated and cumulative risks to consumers, with special emphasis on children. The proposal also includes exposure data tailored specifically to address pesticide handlers is crucial in assessing their risk and thus adequately protecting their health.

ii. *More refined exposure assessments mean clearing understanding of real risks.* EPA's current application and post-application exposure data base is not comprehensive, especially regarding exposures to pesticides in some agricultural or nonagricultural settings. The new data that would be collected under this proposal would allow the Agency to conduct improved exposure

assessments for residential sites and for bystanders in other settings. This will benefit farmers and other workers by allowing EPA to make better informed regulatory decisions that are neither too stringent nor too lenient.

iii. *Clarity and transparency to regulated community means savings.* The enhanced clarity and transparency of the information presented in part 158 should enhance the ability of industry to avoid wasted time and effort. Registrants may save time and money by understanding when studies are needed. This should allow products to enter the market earlier, thus increasing profits. The addition of some data requirements is likely to further communicate to domestic and world-wide marketplaces that pesticide products and items treated with them are safer, thus enhancing the reputation of American agricultural products and registered pesticides as tools for public health, etc.

iv. *Enhanced international harmonization means less duplication.* Data generated as a result of the revised requirements in part 158 would generally be sufficient for the needs of the OECD countries because EPA has harmonized the FIFRA test guidelines with those OECD. As a result, assessments of pesticides that are developed using data under the revised part 158 can be shared worldwide, allowing companies to avoid duplicative efforts to meet the requirements of other countries where the company may also manufacture and sell certain pesticides. This should lead to cost savings for companies that operate in the international market.

However, since EPA continues to allow applicants to submit and use their own study protocols to generate data that they subsequently submit to EPA, and there are differences in the mandate and authorities between EPA and OECD countries, the data submitted to EPA under part 158 would be expected to satisfy OECD standards under most circumstances, but perhaps not in all cases.

v. *Better informed users means informed risk-reduction choices.* Better regulatory decisions resulting from the proposed changes should also mean that the label will provide better information on the use of the pesticide. A pesticide label is the user's direction for using pesticides safely and effectively. It contains important information about where to use, or not use, the product, health and safety information that should be read and understood before using a pesticide product, and how to dispose of that product. This benefits users by enhancing their ability to obtain pesticide products appropriate to their needs, and to use and dispose of products in a manner that is safe and environmentally sound. Farmers (as well as other applicators) may benefit from label information based on the data submitted to the extent it helps inform their decisions about whether or how to use particular pesticides to avoid potential exposure to people or the environment from residues on treated crops or through off-site movement.

vi. *EPA information assists other communities in assessing pesticide risks.* Scientific, environmental, and health communities find pesticide toxicity information useful to respond to a variety of needs. For example, medical professionals are concerned about the health of patients exposed to pesticides; poison control centers make use of and distribute information on toxicity and treatment associated with poisoning; and scientists use toxicity information to characterize the effects of pesticides and to assess risks of pesticide exposure. Similarly those responsible for protection of non-target wildlife need reliable information about pesticides and assurance that pesticides do not pose an unreasonable threat. The proposed changes will help the scientific, environmental, and health communities by increasing the breadth, quality, and reliability of Agency regulatory decisions by improving their scientific underpinnings. In turn, the companies will be able to improve their ability to make appropriate decisions and take useful actions.

C. How Will this Proposal Affect Existing Registrations?

This proposal concerns prospective data requirements for future registrations of pesticides. That is, these proposed data requirements would apply to all new registrations of pesticides after the rule is finalized. The Agency does not intend to apply these requirements retrospectively to all existing pesticide registrations. While the intended future applicability of this proposed rule is to new applications, the Agency may find it necessary to call-in some data on certain existing registrations, as warranted by emerging risks of concern on particular pesticides or as a result of possible future programmatic changes and priorities on existing pesticides.

VI. Overview of Proposed Changes

A. Phased approach

This proposal is the first in a series of revisions aimed at comprehensively updating EPA's pesticide data requirements. The data requirements discussed in this proposal pertain to conventional pesticides. Future proposals will address data requirements for antimicrobial pesticides, biochemical and microbial pesticides, inert ingredients in pesticide products, and product performance data requirements.

B. Organizational changes

Part 158 is currently divided into four subparts:

- Subpart A, General Provisions
- Subpart B, How to Use Data Tables
- Subpart C, Product Chemistry Data Requirements
- Subpart D, Data Requirements Tables

EPA proposes to reorganize part 158 to more closely correspond with the Office of Prevention, Pesticides, and Toxic Substances (OPPTS) Harmonized Guidelines, primarily by creating a series of new subparts to replace subpart D. Each subpart will address an individual scientific discipline or data type. In this preamble, EPA will refer to the proposed new subpart and section designations when discussing the data requirements. Table 1 below provides a cross-reference between the current and proposed new subparts. Future new subparts are included for information.

TABLE 1.—PART 158: PROPOSED CHANGE TO SUBPART DESIGNATIONS

Current Regulation and Title	Proposed Regulation and Title
Subpart A: 158.20 General Provisions	Subpart A: 158.1 General Provisions
Subpart B: 158.100 How to Use Data Tables	Subpart B: 158.100 How to Use Data Tables
Subpart C: 158.150 Product Chemistry	Subpart D: 158.300 Product Chemistry
Subpart D: 158.240 Residue Chemistry	Subpart O: 158.1200 Residue Chemistry
Subpart D: 158.290 Environmental Fate	Subpart N: 158.1100 Environmental Fate
Subpart D: 158.340 Toxicology	Subpart F: 158.500 Toxicology
Subpart D: 158.390 Reentry Protection	Subpart K: 158.800 Post-application Exposure
Subpart D: 158.440 Spray Drift	Subpart R: 158.1400 Spray Drift

TABLE 1.—PART 158: PROPOSED CHANGE TO SUBPART DESIGNATIONS—Continued

Current Regulation and Title	Proposed Regulation and Title
Subpart D: 158.490 Wildlife and Aquatic Organisms Subpart D: 158.590 Nontarget Insects	Subpart E: 158.400 Terrestrial and Aquatic Nontarget Organisms
Subpart D: 158.540 Plant Protection	Subpart J: 158.700 Plant Protection
Subpart D: 158.640 Product Performance	Subpart G: 158.600 Product Performance
Subpart D: 158.690 Biochemical Pesticides	Subpart L: 158.900 Biochemical Pesticides
Subpart D: 158.740 Microbial Pesticides	Subpart M: 158.1000 Microbial Pesticides
	Subpart P: 158.1300 Pesticide Management and Disposal (Reserved) Subpart U: 158.1500 Applicator Exposure Subpart V: 158.1600 Inert Ingredients (Reserved) Subpart W: 158.1700 Antimicrobials

Further, EPA proposes to remove the current Appendix A, which contains a compendium of pesticide use sites and use categories to help determine data requirements. This will be separately issued and maintained as a guidance document.

C. ''New Requirement'' Vs.''Newly Codified Requirement.''

FIFRA is a licensing statute, under which regulatory decisions on the registrability of an individual product is based upon data specific to the product and its uses. EPA is authorized to require the submission of data that it needs to make the registration decision in the context of any individual application for registration, amended registration or reregistration. EPA may also impose a data requirement after registration in order to maintain the registration, using specific Data Call-In (DCI) authority of FIFRA sec. 3(c)(2)(B).

Since 1984, when part 158 was first promulgated, EPA's data requirements have evolved as the general scientific understanding of the potential hazards posed by pesticides has grown. Most of the data requirements contained in this new proposal have been applied on a case-by-case basis to support individual applications, or imposed via a DCI on all registrants of similar products. Thus EPA's actual data requirements have progressed as scientific understanding and concerns have evolved, but part 158 data requirements have not been updated to keep pace.

The result of this regulatory lag is that EPA regards many data requirements in today's proposal to be ''newly codified requirements,'' routinely applied in practice on a case-by-case basis but simply not codified in the CFR. However, because they have not been codified, they are considered to be ''new requirements'' never before imposed on the regulated industry. For the purposes of this proposal, EPA has evaluated the costs and burdens of all proposed requirements, whether ''new'' or ''newly codified '' against the data requirements as originally promulgated in 1984, termed ''existing requirements.'' Many of these studies can be categorized as rarely to infrequently required.

In this preamble, EPA is proposing new and revised data requirements that encompass all three categories of requirements:

1. EPA is proposing ''new requirements,'' never before imposed on any registrant.

2. EPA is proposing ''newly codified requirements,'' which have been applied on a case-by-case basis, but are not in the CFR.

3. EPA is proposing revisions to ''existing requirements.''

D. Types of Revisions Being Proposed

Part 158 is a massive and complex set of tables that describe pesticide data requirements. Each data requirement is currently established and its scope and applicability defined according to a number of parameters. Having comprehensively evaluated its data requirement parameters, EPA is proposing changes in all areas of data requirements. Some of these changes are clarifications or housekeeping changes without cost or burden, others have the effect of increasing or decreasing the burden of the data requirement. The types of changes may be broadly categorized as follows:

1. *Substantive changes*—i. *Addition of a requirement.* This encompasses both ''new requirements'' and ''newly codified requirements.'' For example, EPA is proposing a ''new requirement'' for immunotoxicity testing. On the other hand, data requirements for applicator exposure (subpart U) are entirely ''newly codified.''

ii. *Elimination of a requirement, sometimes with substitution of a new requirement.* For example, EPA is wholly eliminating the requirement for seed germination testing. By contrast, the existing requirement for a battery of mutagenicity studies is being eliminated in favor of a specific set of mutagenicity studies.

iii. *A change to the number or type of species that must be tested.* For example, EPA proposes to require acute avian toxicity testing on an additional passerine species in some instances. EPA also proposes to require that certain toxicity studies be conducted routinely with two species instead of one.

iv. *A change in the conditionality of the test requirement.* For example, EPA is proposing to change a number of requirements from conditionally required to fully required, or vice versa. In some cases, this change is a minor change in the actual frequency (and burden) of the requirement. In other cases, the change may represent a substantive increase in frequency of requirement.

v. *A change to the use patterns to which a data requirement applies.* As described elsewhere, EPA proposed to increase the number of use pattern descriptors from 9 to 15. In some cases, EPA proposes to extend requirements currently limited to food uses to nonfood uses, *e.g.*, prenatal developmental toxicity studies. A second example would be a proposed expansion of certain studies into greenhouse and indoor use patterns, for example, avian oral toxicity requirements.

vi. *A change to the test substance to be used.* Typical test substances include the technical grade of active ingredient (TGAI), the manufacturing-use product, the end-use product, and a ''typical product.'' For example, EPA proposes to require primary eye and primary dermal irritation, and dermal sensitization testing using the TGAI in addition to the end-use product.

vii. *A clarification in the notes describing the test.* For example, EPA is proposing in a test note that analytical methods for residue chemistry and environmental fate be validated by an independent laboratory.

2. *Technical changes having no substantive effect*—i. *Relocation of a requirement.* For example, EPA proposes to move the magnitude of residues in rotational crops data requirement from environmental fate requirements to residue chemistry requirements.

ii. *A change to the title of a data requirement.* For example, EPA proposes to rename the ''teratogenicity'' data requirement to ''prenatal developmental toxicity'' to more accurately reflect the nature of the study.

iii. *Subdividing an existing requirement to create two separate entries.* For example, EPA proposes to separately list the storage stability requirement for residue samples. This requirement is currently included in the plant and animal metabolism data requirement. A change of this nature is intended to highlight an aspect of a test requirement for the regulated community.

iv. *Merging two data requirements into a single requirement.* For example, EPA proposes to merge the terrestrial field dissipation study with the long-term field dissipation study because both studies provide similar information.

Each data requirement for which a revision is proposed is discussed in detail in subsequent units of this preamble. Readers are referred to the table in Unit XXIII. for a line-by-line listing of every current and proposed data requirement and the types of changes proposed. If no change is proposed, the table contains a notation to that effect.

VII. General Provisions of Part 158 (Subpart A)

A. General

Subpart A serves as an introduction to the data requirements in part 158. As proposed, current material has been substantially revised to be more concise and easier to understand. EPA has eliminated much of the redundancy in current subpart A and streamlined the remaining material. Unless otherwise superseded by part 174, the regulations of this part apply to plant-incorporated protectants.

1. *New material.* New content has been added to subpart A. Specifically, EPA has added new § 158.3 containing definitions relevant to part 158 as a whole. In this proposal, EPA has referred to statutory definitions in FIFRA and FFDCA, and has included only a single new definition, that of ''applicant.'' This definition is intended to provide an inclusive term that covers all persons who submit data to the Agency for any purpose, including applicants for registration, reregistration, or experimental use permit under FIFRA, petitioners for tolerance or exemption under FFDCA, and registrants who are required to submit data to maintain registration. The term ''applicant'' is proposed to be used for all such persons. The definition is drawn from the definition of ''application for research or marketing permit,'' in 40 CFR 160.3, which also relates to data development. EPA requests comment on whether additional definitions are needed.

2. *Disposition of current subpart A material.* The following sections of current subpart A are proposed to be deleted or substantially revised. The following Table 2 explains each section.

TABLE 2.—DISPOSITION OF CURRENT SUBPART A MATERIAL

Section	Title	Disposition
158.20	Overview	Paragraph (a) deleted Paragraph (b). Content contained in proposed § 158.1, Purpose and Scope. Paragraph (c) deleted.
158.25	Applicability of data requirements	Deleted as redundant or unnecessary. Applicability of this part to various regulatory actions is contained in proposed § 158.5
158.30	Timing of the imposition of data requirements	Deleted as unnecessary and not relevant. This section addresses approval of registration actions, which is properly covered in part 152, and is not relevant to data requirements.
158.32	Format of data submissions.	Retained and revised. Discussed in Unit VII.B.
158.33	Procedures for claims of confidentiality of data.	Retained and revised. Discussed in Unit VII.C.
158.34	Flagging of studies for potential adverse effects.	Retained. Criteria revised.
158.35	Flexibility of the data requirements	Deleted as redundant. Mainly contains cross-references to similar material elsewhere in part 158.
158.40	Consultation with the Agency.	Deleted. Consultation with the Agency is encouraged in several sections of proposed part 158.
158.45	Waivers	Retained and revised. Discussed in Unit VII.E.
158.50	Formulator's exemption	Information to be relocated to 40 CFR 152.85, which covers the formulator's exemption.
158.55	Agricultural vs. Non-agricultural pesticides	Deleted as unnecessary. Material is covered in individual subparts of proposal, which are organized by agricultural and no-agricultural use patterns.
158.60	Minor uses	Deleted as unnecessary. Definitions and minor use policies are largely governed by statutory mandates and priorities, not regulatory policies.
158.65	Biochemical and microbial pesticides	Deleted. Material will be considered for inclusion in future revisions of biochemical and microbial data requirements.
158.70	Acceptable protocols	Revised.

TABLE 2.—DISPOSITION OF CURRENT SUBPART A MATERIAL—Continued

Section	Title	Disposition
158.75	Requirements for additional data	Paragraph (a) retained. Paragraph (b) deleted as unnecessary. This material is covered by paragraph (a).
158.80	Acceptability of data	Paragraph (a) moved to § 158.70(a) - now refers to ''cited.'' Paragraph (b) deleted. Paragraph (c) retained. Paragraph (d) revised.
158.85	Revision of data requirements and guidelines	Deleted as unnecessary. Guideline references are contained in tables in each subpart.

B. Format of Data Submissions

EPA proposes to reorganize for clarity the data submission requirements of § 152.32. EPA would eliminate descriptions of EPA assignment of MRID numbers, as this internal action does not bear upon applicant requirements. Applicants would continue to format data submissions in support of regulatory actions according to current Agency procedures. The proposed rule makes clear that administrative non-data elements of a submission (forms, labels, and correspondence) are not subject to formatting requirements.

The Agency also proposes to eliminate specific media and copy requirements from the regulatory text because these requirements are subject to change as the Agency implements new strategies to reduce the paperwork burden on data submitters and to simplify the submission process. The Agency intends to provide updated guidance in a new PR Notice that will supersede PR Notice 86–5. EPA has a web page that provides guidance for both paper and electronic data submission.

After a series of pilots EPA has developed a standard for electronic submission of data using Adobe Acrobat Portable Document Format and related tools for pesticide data submitters to create electronic versions of documents. Extensive guidance has been developed and posted on the EPA web page dedicated to electronic submissions(*http://www.epa.gov/oppfead1/edsgoals.htm*). As experience is gained, and in consultation with stakeholders, EPA intends to refine its guidance.

Registrants should note that regulations in part 159 concerning FIFRA sec. 6(a)(2) submissions require that such data be formatted according to the requirements of this section.

C. Confidential Business Information

EPA proposes to clarify its policies on confidentiality claims asserted by submitters and on the release of information by the Agency. Section 158.33 discusses information that may be claimed as confidential and the procedures for asserting such a claim. It also discusses information that may be released by EPA, and circumstances under which such information can be released. Any release of information by EPA would be in accordance with FIFRA sec. 10, FFDCA sec. 408, and EPA regulations under the Freedom of Information Act (5 U.S.C. 552) found in 40 CFR part 2. The revisions to procedures for asserting confidentiality claims would not apply to data submitted to the Agency before the date of promulgation of this rule. Further regulatory provisions regarding confidentiality can be found at 40 CFR part 2.

1. *Confidentiality of 408 information.* EPA also proposes to implement the revised confidentiality provisions in FFDCA sec. 408(i). Prior to the changes made in FFDCA by FQPA in 1996, confidentiality of information submitted in support of a tolerance or exemption was governed by old sec. 408(f), which made all such information confidential until publication of a regulation establishing a tolerance or exemption (unless the submitter explicitly waived confidential protection). This section was replaced in 1996 by current sec. 408(i), which provides in part, ''Data and information that are or have been submitted to the Administrator under this section or sec. 348 of this title in support of a tolerance or an exemption from a tolerance shall be entitled to confidential treatment for reasons of business confidentiality and to exclusive use and data compensation to the same extent provided by secs 3 and 10 of the Federal Insecticide, Fungicide, and Rodenticide Act.'' EPA has never formally interpreted the meaning of sec. 408(i) with respect to confidential information.

The likely intent of Congress was to accord information submitted in support of a tolerance or exemption the same confidentiality protections that apply to data submitted under FIFRA, especially considering the extent to which FIFRA and FFDCA were intertwined more closely by FQPA. Treating information submitted under the two statutes identically means that they are subject to the same protections (*e.g.*, restrictions on disclosure of entire studies to multinational corporations in accordance with FIFRA sec. 10(g)) and the same disclosure requirements (*e.g.*, mandatory public availability of safety and efficacy information in accordance with FIFRA 10(d)(1)). In fact, this discussion may be largely academic, because EPA expects that nearly all data submitted under part 158 in support of a tolerance or exemption will also be information submitted under FIFRA. The only exception would pertain to import tolerances or exemptions for pesticides that are not used in the United States, submissions which are uncommon. All references in this preamble to FIFRA sec. 10 are therefore intended to apply equally to information submitted pursuant to FFDCA 408.

2. *Safety and efficacy information.* Information pertaining to the safety and efficacy of registered pesticides must in most cases be made available to the public. The existing provisions in 40 CFR 158.33 regarding the confidentiality of safety and efficacy information have in some cases been unclear to registrants and applicants, resulting in confusion regarding what information is claimed as confidential. EPA seeks to clarify these provisions, and to clear up some long-standing misconceptions as to the eligibility of inert ingredient and process information for confidential treatment.

FIFRA sec. 10(d)(1) provides that ''information concerning the objectives, methodology, results, or significance of any test or experiment performed on or with a registered or previously registered pesticide or its separate ingredients, impurities, or degradation products, and any information concerning the effects of such pesticide on any organism or the behavior of such pesticide in the environment, including, but not limited to, data on safety to fish and wildlife, humans and other mammals, plants, animals, and soil, and studies on persistence, translocation

and fate in the environment, and metabolism'' must be made available to the public. EPA considers metabolites to be a form of ''degradation product'' within the meaning of sec. 10(d)(1).

Excepted from that mandatory disclosure requirement is certain information pertaining to manufacturing and quality control processes and to inert ingredients, which is given qualified protection under FIFRA secs. 10(d)(1)(A), (B), or (C). This exception has been frequently misinterpreted to mean that all such information is made categorically confidential by sec. 10(d)(1). In fact, as decided by the *District Court for the District of Columbia in NCAP v. Browner*, 941 F.Supp. 197, 201 (D.D.C. 1996), the statute makes information subject to FIFRA sections 10(d)(1)(A), (B), or (C) neither categorically confidential nor categorically public. Instead, the information may be entitled to confidential treatment, but only if it meets the requirements of sec. 10(b) (generally, trade secrets and information whose disclosure is likely to cause substantial harm to the competitive position of the submitter).

EPA believes that, with the exception of information pertaining to a pesticide that has never been registered, all information submitted in accordance with part 158 (including information submitted in connection with an application for a tolerance or exemption) constitutes safety and efficacy information subject to sec. 10(d)(1). All of the information subject to part 158 concerns ''the effects of such pesticide on any organism or the behavior of such pesticide in the environment.'' This includes not only studies regarding hazard and fate, but also information such as product chemistry, which is collected by the Agency for the very purpose of determining the effects of the pesticide on organisms and its behavior in the environment.

In addition to providing submitters with an opportunity to designate information as subject to one of the exceptions in FIFRA secs. 10(d)(1)(A), (B), or (C) (a feature also contained in the current version of § 158.33), EPA proposes to include a provision that all information that has not been so designated and that pertains to a registered or previously registered pesticide be deemed non-confidential by operation of law, without further notice to the submitter (subject to the requirements of sec. 10(g) regarding disclosure to multinational entities). This provision would not apply to information that was submitted prior to May 4, 1988, the effective date of the current regulation contained in § 158.33, and thus the first time that claims under sec. 10 (d)(1)(A), (B), or (C) were required to be identified.

3. *Information pertaining to unregistered pesticides.* Although safety and efficacy information (which by definition pertains only to registered or previously registered pesticides) is made publicly available by statute, if the information pertains to unregistered pesticides (including both applications for new active ingredients and import tolerances for pesticides used only outside the United States) it is not subject to the same mandatory disclosure requirement. Such information may be entitled to confidential treatment if it meets the requirements of sec. 10(b). In practice, EPA believes that information relating to the effects of unregistered pesticides that is not within one of the exceptions in FIFRA sec. 10(d)(1)(A), (B), or (C) will seldom meet this test. Much of the information in studies is valuable only to the extent that it can be used for registration/tolerance purposes, and protection from unauthorized submission or citation of a study by persons other than the submitter is provided by the FIFRA and FFDCA data compensation provisions and by FIFRA sec. 10(g). Moreover, because such information becomes publicly available once the pesticide is registered, competitors will eventually be able to get access to the information. Thus, confidentiality should normally be appropriate only when disclosure of the information prior to registration would give competitors an advance look at information that they could use to their advantage.

At the same time, the period prior to registration is of special importance for public participation in the registration process. Under FIFRA sec. 3(c)(4), EPA publishes a **Federal Register** notice announcing receipt of an application for registration of a product involving a new active ingredient or changed use pattern, and gives the public an opportunity to comment on the application. Implicit in the opportunity to comment is the availability of sufficient information to evaluate the risks and benefits of the product. Although requests for pre-registration information may be made under the Freedom of Information Act, the amount of time involved in contacting the submitter to clarify claims, obtaining substantiation of the confidentiality claim, and making a final determination on the claim make it very difficult for the public to get access to important information on a timely basis.

Because of the possibility that some pre-registration information may be legitimately confidential, EPA does not believe that it can categorically determine all such information to be non-confidential. The provisions in this proposal requiring the submitter to specify which information is claimed as confidential will simplify access to information not so claimed, but EPA is soliciting comment on other mechanisms to facilitate public access to pre-registration information.

4. *Confidentiality claims for plant-incorporated protectant information.* Part 174 was incorporated into 40 CFR effective September 17, 2001. The regulations in part 158 apply to plant-incorporated protectants unless otherwise superseded by part 174. In addition to complying with the requirements of § 158.33, any confidentiality claims for information subject to 40 CFR part 174 (plant-incorporated protectants) must be substantiated at the time of submission as described in § 174.9.

5. *Disclosure of data to multinational entities.* Also included is a proposed provision governing the release of data to foreign or multinational pesticide companies. Under sec. 10(g) of FIFRA, EPA requires that any person requesting information from the Agency affirm that he or she is not an ''entity engaged in the production, sale, or distribution of pesticides in countries other than the United States or in addition to the United States'' and that the information will not be disclosed to such an entity. The requirement for such an affirmation applies to all data received by the Agency under FIFRA (and FFDCA) and is not limited to confidential business information.

In Class Determinations 3–85 (50 FR 48833, November 27, 1985) and 1–99 (64 FR 70019, December 15, 1999) EPA elucidated the criteria for determining whether information and documents derived from studies or reports submitted to the agency are subject to the restrictions of FIFRA sec. 10(g). In order to be outside the scope of sec. 10(g), documents must not (1) ''contain or consist of any complete unpublished report submitted to EPA '' or (2) ''contain or consist of excerpts or restatements of any such report which reveal the full methodology and complete results of the study, test, or experiment, and all explanatory information necessary to understand the methodology or interpret the results.'' (50 FR 48834). Although the application of these class determinations is limited to data reviews created by the Agency (3–85) and information regarding unreasonable adverse effects of

pesticides on the environment submitted in connection with sec. 6(a)(2) of FIFRA (1–99), the rationale behind the class determinations applies to all data which meet the criteria quoted in this paragraph. In order to facilitate the timely release to the public of important safety and efficacy information beyond that contained in data reviews and 6(a)(2) notices, EPA is proposing to codify these determinations with respect to all information submitted in accordance with part 158.

6. *Release to state and foreign governments with consent.* EPA also is including in this proposal a provision to facilitate the release and exchange of information with State and foreign regulatory agencies. In an effort to promote harmonization and to conserve resources through work share programs, the exchange of data often is beneficial and desirable. Applicants would have the option of signing a statement authorizing the Agency to release information contained in their documents for such purposes. Although most governments provide protection for confidential information, EPA cannot guarantee how a particular government would treat specific information disclosed to it. Consequently, the submitter should be aware of any risk involved before granting consent to disclosure. However, EPA would not view disclosure to a government that protected confidential information as otherwise waiving confidential treatment for the information.

D. Flagging Criteria

EPA proposes to revise the flagging requirements of § 158.34, established in 1985, without changing the substance of the requirement. Currently, applicants for registration and amended registration, and submitters of data under FIFRA sec. 3(c)(2)(B) are required to flag certain toxicology studies that show results potentially indicating an adverse effect. EPA proposes to make minor revisions to update and clarify the criteria to encompass the new types of toxicology studies being proposed today. Specifically, EPA proposes to:

1. Reduce the number of study criteria from 11 to 7 by combining certain studies under one criterion. The new criteria would eliminate distinctions between subchronic and chronic studies in most cases.

2. Combine reproductive, prenatal developmental toxicity and developmental neurotoxicity studies under one criterion to better focus on effects on children and infants.

3. Consolidate the criteria that address the No-Observed-Adverse-Effect Levels (NOAEL) into a single criterion covering all studies from which NOAELs are derived. In so doing, EPA would change references to cholinesterase inhibition to ''acute toxicity.'' This change acknowledges that NOAELs are now derived for a number of acute toxicity effects, not just cholinesterase inhibition. In a similar vein, EPA would eliminate the specific ''less than 10X'' and ''less than 100X'' triggers for NOAEL study flagging in favor of a more general description of ''less than the current NOAEL.'' Both of these changes could result in more studies being flagged.

4. Update the guidelines references, and terminology, *e.g.*, teratogenicity studies are now called prenatal developmental toxicity studies; the ADI is now referred to as the RfD. EPA believes that these revisions to the criteria will simplify the application of the criteria by submitters, even though additional studies may be required to be flagged.

E. Waivers

EPA proposes to reformat its waiver process, currently contained in § 158.45, but to retain its provisions. This proposal retains the flexibility of the current provisions for applicants to request, and EPA to evaluate, the need for data on a case-by-case basis depending on individual chemicals and use patterns. One of the benefits of updating part 158 as proposed today is that the improvements in clarity and transparency of the data requirements will greatly assist both the Agency and applicants in addressing data waivers.

1. *Waiver requests submitted as part of an application for registration.* Waiver requests submitted in conjunction with an application for registration, amended registration, experimental use permit, or petition for tolerance are considered in the context, and in the same time frame, as the application is considered, based upon the application review period in FIFRA sec. 33. The review periods currently range from 90 days for minor amendments to as much as 3 years for new chemical applications. Consideration of waiver requests (and there may be multiple requests in a single application) is done by Agency scientists when the application is reviewed scientifically.

2. *Waiver requests submitted in response to Data Call-Ins for studies that are required in part 158.* In the case of DCIs for data requirements that are contained in part 158, EPA believes that it will be able to make waiver decisions in a reasonably prompt timeframe since the need for the data has been established, the criteria upon which the data are required (use pattern, exposure pattern, chemical characteristics, etc.) have been elaborated, and the conditionalities associated with its imposition have been carefully considered in the development of this proposal. In other words, much of the evaluative process associated with a data waiver has already been done. Thus EPA will be able to judge an adequately supported waiver request against these existing factors to determine whether a waiver can be granted.

Moreover, the improved transparency of the requirements and conditions in new part 158 means that an applicant will be able to ascertain with reasonable certainty the likelihood that EPA would consider favorably a waiver request. EPA believes that improved clarity will also reduce the number of frivolous, inappropriate, or ill-supported waiver requests. Thus, EPA believes it will be able to respond in a reasonable period of time to a waiver request. If EPA requires a lengthy period to reach a decision on a waiver request which is denied, the Agency will generally consider time extensions to accommodate legitimate and reasonable registrant needs, whether to define acceptable protocols, evaluate alternative tests that might satisfy the Agency's requirements, or allow for consideration of laboratory capacity.

F. Minor Uses

Current § 158.60 outlines a number of non-regulatory policies EPA adopted to limit the economic impact of data requirements on minor use products while ensuring that the Agency had adequate data to assess the potential risks and benefits of these pesticides. Because minor use policies by themselves are somewhat fluid and subject to change periodically, EPA proposes to remove § 158.60. EPA, however, remains committed to the minor use program by imposing the mandates contained in FIFRA that relate to minor uses, such as extending exclusive use of minor use data, granting minor use waivers, and expediting minor use registrations. The Agency believes that tiered testing, outlined elsewhere in this proposal, coupled with its waiver policy in § 158.45 and priority review status, limit the economic burden for all pesticides by ensuring that registrants are required to develop only those studies that are essential for an appropriate safety evaluation.

VIII. How to Use the Data Tables (Subpart B)

EPA proposes to revise subpart B to update use patterns and clarify the steps needed to determine the appropriate data requirements from the tables in subparts, D, E, F, J, K, N, O, and U. Pesticide use patterns that are used to determine required testing have been revised for all of the data requirements tables to reflect the expanded use patterns contained in this proposal (see below).

A. Expanded Use Patterns

EPA proposes to subdivide the current 9 major use patterns listed in Appendix A of part 158 to 15 to more fully address nonagricultural uses. The revised use patterns would be terrestrial food crop, terrestrial feed crop, and terrestrial nonfood crop; aquatic food crop, aquatic nonfood crop, aquatic nonfood outdoor use and aquatic nonfood industrial use; greenhouse food crop and greenhouse nonfood crop; forestry; residential outdoor; indoor food; indoor nonfood; indoor medical; and indoor residential use. As mentioned above, the Agency proposes to remove the Pesticide Use Index (Appendix A) from the regulations because it is not a requirement. Instead, the Index will become a separate guidance document and placed on EPA's website and made available to the public. A guidance document would be easier to update and would provide the regulated community with the most current information.

B. Clarifying How to Use the Data Tables

Subpart B would contain a step-wise process to assist the applicant in determining the data needed to support its particular product. As with current practice, the actual data and studies required may be modified on an individual basis to fully characterize the use and properties of specific pesticide products under review. While EPA is attempting to assist the applicant in this subpart, it is important to emphasize that it is the applicant's obligation under FIFRA to demonstrate that an individual product meets the standard under FIFRA and/or FFDCA. Accordingly, applicants are encouraged to consult with the Agency on the appropriate data requirements as proposed here as they relate to their specific product prior to and during the registration process.

EPA is continuing its current system of identifying the applicability of data requirements in the data tables. Because of the variety of chemicals and use patterns, and because EPA must retain flexibility to tailor data requirements to its needs, it uses only qualitative descriptors in the tables. These are used for convenience to make the table format feasible, but serve only as a general indication of the applicability of a data requirement. In all cases, the test notes referred to in the table must be consulted to determine the actual applicability of the data requirement.

The table descriptors NR (not required), R (required), and CR (conditionally required) can be viewed as markers along a spectrum of the likelihood that the data requirement applies. The use of R does not necessarily indicate that a study is always required, but that it is more likely to be required than not. The use of CR means a study is less likely to be required. Although only an approximation, if percentages were to be assigned, R could be viewed as representing the range of 50% to 100% and CR the range up to 50%. EPA welcomes comment on ways to characterize the data requirements that would better serve applicant needs.

EPA is continuing its longstanding system of identifying test substances in the tables. The standard descriptors of test substance are the following:

1. The technical grade of active ingredient (TGAI), used when evaluating the inherent toxicity or chemical characteristics of a pesticide.
2. The manufacturing use product (MP), used in certain product chemistry tests, usually for labeling purposes.
3. The pure active ingredient (PAI), used in certain product chemistry tests requiring extremely basic chemical properties or manufacturing process information.
4. The pure active ingredient, radioactive (PAIRA), used primarily in residue chemistry studies when residues at very low levels (ppm) must be quantified in plant or animal tissue.
5. The end-use product (EP), used as the test substance when the Agency wants to refine its hazard or chemical profile based on actual concentrations, or needs to determine the impact of added inert ingredients on the hazard or chemical profile.
6. The typical end-use product (TEP), used as a representative product in tests that might otherwise require duplicative testing of a number of EPs.

Where changes in the test substance are proposed, such changes are described in the discussion of each proposed revision. EPA welcomes comment on its test substances and how the Agency uses them in a testing regimen. Such comments should be made in the context of the specific data requirement for which changes are proposed.

C. Identifying Data for Experimental Use Permits (EUPs)

Finally, the Agency is requesting comment on the best way to identify data requirements for EUPS. Some people believe that the brackets indicating what data requirements also apply to EUPs in the current data tables complicate the tables with extraneous symbols and codes. In an effort to make the data tables simpler and easier for an applicant to understand, one suggestion is to separate the EUP data requirements from the main data tables and make them a stand-alone table. Revised EUP data requirements could be housed in 40 CFR part 158 (data requirements) or in part 172 (EUP requirements). As part of this proposal, EUP data requirements for each discipline have been identified either in the regulatory text accompanying the data table or, as brackets, within the body of the table, itself. In general, the Agency proposes to retain the existing data requirements for EUPs with a few minor changes in the areas of environmental fate and ecological effects. The Agency is soliciting opinions on this approach or other approaches that may prove more efficient and useful to the applicant. If an alternative approach is accepted, the Agency may in the final rule, reformat the regulatory text or data tables.

D. Test Guidelines

The guidelines for the environmental fate series are currently being updated and where applicable, harmonized with the guidelines established by the OECD. Therefore, the Agency is showing the current guideline numbers in the preamble, regulatory text, and tables. If, before the final rule has been promulgated, these guidelines have been issued, EPA will insert the new guideline numbers in the Final Rule.

E. Purposes of the Registration Data Requirements

The Agency proposes to retain the material currently in § 158.202 Purposes of the registration data requirements in subpart D, Data Requirements Tables. Since a series of new subparts will replace subpart D, this material will be moved to subpart B.

IX. Product Chemistry Data Requirements (Subpart D)

A. General

The Agency uses product chemistry information to determine whether impurities of toxicological or environmental concern are present in pesticides and formulated products.

Product chemistry data requirements are comprised of product identity and composition data along with the physical and chemical characteristics of a pesticides, plus any intentionally added ingredients and impurities in the final pesticide product. Included in this subpart are the specific, detailed requirements for product identity and chemical analysis. The Agency is proposing two additional data requirements and other minor revisions that would clarify the applicability of existing requirements. For example, the Agency proposes to revise the definition of an active ingredient and end-use product to include nitrogen stabilizers, which were added to the definition of ''pesticide'' in 1996.

The Agency proposes to list entries in the data requirements table for product identification, composition, analysis, and certification of limits requirements. These requirements are currently contained in § § 158.155 through 158.180, and are proposed to be retained unchanged as new § § 158.320 through 158.355. Inclusion in the table for product chemistry is for the convenience of applicants--the requirements themselves are not affected by including them in the table. The test notes refer applicants to the subsequent section that discuss the requirements in detail.

The Agency's current policy as described in Pesticide Registration Notice 98–1 (January 12, 1998) allows applicants and registrants to submit a summary of the physical and chemical properties of non-integrated pesticide products, EPA Form 8570–36, rather than submit the studies upon which these data are based. The self-certification statement (EPA Form 8570–37) must be signed and dated by the applicant certifying that the submitted information was conducted in full compliance with the regulations (Attachment 2 to PR notice 98–1). The PR notice applies to applications for registration of manufacturing-use and end-use products of all pesticide products produced by a non-integrated formulation system.

B. Proposed Product Chemistry Data Requirements

1. *Newly imposed data requirements.* None.

2. *Newly codified data requirements*—i. *UV/visible light absorption.* The Agency proposes to add a requirement for data on the ultraviolet (UV)/visible light absorption in the 200–800 nanometers wavelength range (guideline 830.7050) as part of the basic data in the characterization and identification of a compound. This information will be used in conjunction with the photodegradation in water study (§ 158.1100) to determine if photodegradation is a possible route of dissipation in the environment. In order for a pesticide to undergo direct photolysis in the environment, it must absorb energy in the wavelength range emitted by sunlight. While the UV/visible light absorption spectrum will indicate whether or not the chemical absorbs in this range and hence may potentially photodegrade, it does not actually measure the photodegradation rate or identify photodegradates. Accordingly, test note 2 for the photodegradation study states that the photodegradation in water study will not be required when the electronic absorption spectra, measured at pHs 5, 7, and 9, of the chemical and its hydrolytic products, if any, show no absorption or tailing between 290 and 800 nm.

ii. *Particle size, fiber length, and diameter distribution.* The Agency proposes to add the conditional requirements for data on particle size, fiber length, and diameter distribution (guideline 830.7520). This study would be conditionally required for water insoluble test substances ($<10^{-6}$ g/l) and fibrous test substances with diameter ≥0.1 µm. Data from this study are needed in the environmental fate assessment to estimate potential chemical drift to nontarget areas.

3. *Revised data requirements*—i. *Stability to temperatures, metals, and metal ions.* The Agency proposes to change the requirement for stability data (guideline 830.6313) from ''required'' to ''conditionally required.''Data on the stability to metals and metal ions is required only if the active ingredient is expected to come in contact with either material during storage. This proposed change does not alter the nature of the requirement.

ii. *Explodability.* The Agency proposes to change the requirement for explodability data (guideline 830.6316) from ''required'' to ''conditionally required.'' Since pesticides do not typically fall under this category, these data are only required for products that are potentially explosive. This proposed change does not alter the nature of the requirement.

iii. *Partition coefficient (n-octanol/water).* The Agency proposes to change the requirement from ''conditionally required'' to ''required'' (guidelines 830.7550, 830.7560, and 830.7570). The Agency is requiring this study because the majority of currently registered pesticides are organic non-ionic chemicals that are not expected to significantly hydrolyze or solubilize in water. In the event a chemical fully hydrolyzes or is completely soluble in water, this data requirement would be waived. This proposed change does not alter the nature of the requirement nor the conditions under which it is imposed.

iv. *Density, dissociation constant, and vapor pressure.* The Agency proposes to add test notes for the data requirements for density/relative density/bulk density (guideline 830.7300), dissociation constant (guideline 830.7370), and vapor pressure (guideline 830.7950) to better identify when these study requirements are applicable. These proposed minor changes do not expand the product chemistry requirement. Instead, they clarify the requirements by specifying which physical states or chemical forms the requirements apply.

X. Terrestrial and Aquatic Nontarget Organisms Data Requirements (Subpart E)

A. General

The Agency uses a tiered system of ecological effects testing to assess the potential risks of pesticides to aquatic and terrestrial vertebrates, invertebrates, and plants. These tests include studies arranged in a hierarchy from basic laboratory tests to applied field tests. The results of each tier are evaluated to determine the potential impacts on fish, wildlife and other nontarget organisms, and to indicate whether further laboratory and/or field studies are needed. These data requirements provide the Agency with ecological effects information, which, in turn, allows the Agency to determine if precautionary statements concerning toxicity or potential adverse effects to nontarget organisms are necessary.

Higher tiered studies may be required when basic toxicity data and predicted exposure levels or environmental conditions suggest the potential for adverse effects. Field data are used to examine acute and chronic adverse effects on captive or monitored populations under natural or near-natural environments. Such studies are required only when the potential for adverse effects is high, based on the results of lower tier studies, or to confirm the need for mitigation measures. In some cases, the results of field studies may give rise to the need for further testing.

B. Proposed Requirements

The Agency is proposing two additional data requirements as well as other minor revisions that would clarify the existing data requirements. In some cases, the proposal is to change the

existing test requirement from ''conditionally required'' to ''required '' or ''not required.'' The data requirements for nontarget insects, formerly in § 158.590, would be moved under this proposal to subpart E to consolidate the data requirements for nontarget organisms. Other changes include changes in test substance, conditions under which the test is required, and clarification of test notes.

In addition, as discussed in more detail in this section, the Agency proposes to require an additional test species for the avian oral toxicity study, because current data requirements may not adequately characterize the risks that pesticides pose to songbirds. The Agency also proposes to conditionally require sediment testing to better assess the effects of sediment bound pesticide residues in aquatic environments. The Agency is proposing to require independent laboratory validation of environmental chemistry methods for terrestrial and aquatic field testing.

Finally, the Agency is proposing to eliminate the requirement for avian dietary testing for indoor and greenhouse uses, and to simplify the test notes for these requirements. The Agency invites comments on all aspects of these data requirements.

1. *Newly imposed data requirements.* None.

2. *Newly codified data requirements.* The Agency proposes to add testing of aquatic organisms exposed to treated sediment to better assess the effects of sediment bound pesticide residues in aquatic environments. Environmental risk estimates should be based on exposure data from the water column, sediment, and pore water (the water occupying space between sediment or soil particles), however, with the exception of field studies, the current data requirements are limited to water column exposures. The effects of sediment bound pesticides (or their degradates) on aquatic environments cannot be accurately assessed from bioassays on compounds suspended in the water column alone. For example, lipophilic or hydrophobic chemicals can dissipate from the water column, but may remain in the aquatic environment adsorbed to sediment. Sediment bound pesticides may differ significantly from pesticides in solution, showing different physical, chemical, and biological properties, chemical partitioning, bioavailability, concentrations in interstitial or pore water, exposure from sediment ingestion and possible manifestations of food chain effects. By serving as a potential pesticide sink, exposure to these compounds may lead to significant environmental risk to a wide variety of fish and aquatic invertebrates which live and feed at the bottom of a lake or stream. Sediment toxicity testing is needed to assess the bioavailability of a sediment bound compound and to characterize the possible impact to sediment dwelling organisms. The Agency does not believe these studies will be commonly required.

EPA's Contaminated Sediment Management Strategy (USEPA 1998) (Ref. 3) has been recently developed to provide a more unified approach to testing and risk assessment of aquatic species which inhabit and feed in the benthic environment. Testing would consist of whole sediment (spiked) tests; testing can also consist of chronic whole sediment toxicity tests and/or sampling for residues and biological monitoring of pesticides in the sediment after exposure. EPA has developed test protocols for chronic whole sediment tests of invertebrates. Test guidelines will be developed from these protocols. Protocols for further tests (*e.g.*, acute pore water tests) and for vertebrate species are under consideration. Registrants are urged to meet with the Agency prior to development of their own protocols.

i. *Whole sediment: acute toxicity to invertebrates, freshwater and marine.* The Agency is proposing to conditionally require data for acute invertebrate sediment testing (guidelines 850.1735 and 850.1740) for terrestrial uses, aquatic food and nonfood outdoor uses, and forestry uses. This study would be required when the soil partition coefficient (K_d) is ≥ 50 mg/L, indicating the ability to absorb to sediment, and if the half-life of the pesticide in the sediment is ≤ 10 days in either the aerobic soil or aquatic metabolism studies. Registrants would need to consult with the Agency on appropriate test protocols.

ii. *Whole sediment: chronic toxicity to invertebrates.* The Agency proposes to conditionally require this study for the same use patterns as the above sediment toxicity tests. The study would be triggered when the estimated environmental concentration is greater than or equal to the acute sediment EC_{50}/LC_{50} or the soil partition coefficient (K_d) is ≥ 50 mg/L, indicating the ability to absorb to sediment; and if the half-life of the pesticide in the sediment is >10 days in either the aerobic soil or aquatic metabolism studies. Registrants would need to consult with the Agency on appropriate test protocols.

3. *Revised data requirements—Avian oral toxicity.* The Agency proposes to require for certain uses, an additional test species for the acute avian oral toxicity study (guideline 850.2100), which currently recommends the use of mallard ducks or bobwhite quail. Testing on a passerine species (*i.e.*, redwing blackbird) would be required for outdoor uses. The Agency is proposing to add this passerine species because of concern in the scientific community that data from tests with mallards or quail may not always adequately characterize the risks that pesticides pose to songbirds. Recent evaluation of the data collected over the past 10 years indicates passerines are more sensitive to pesticides than larger birds such as mallards and quail (which are currently the recommended test species) (Ref. 2) and in 1996, the SAP supported the need for testing on passerines. In addition to comments on the proposed addition of a passerine species for the acute oral toxicity study, the Agency requests comments on whether this species should replace the existing bobwhite/mallard species or otherwise be conditional, and if so what criteria or triggers should be used to determine when the data should be required.

The Agency proposes to revise and simplify the test notes for the avian acute toxicity test. The single current footnote is structurally complex, so EPA has subdivided it into 4 test notes that are easier to understand and apply.

In addition, the Agency proposes to conditionally require testing of the typical end-use product (TEP) of granular and non-granular end-use products because the inherent toxicity of end-use products is better defined by testing the product. End-use products may contain chemicals that enhance efficacy by acting as solvents, stickers, and wetting agents. Although these chemicals are listed as inerts, their individual toxicity or combination with one another or the active ingredient (a.i.), may be more toxic than the technical grade of the active ingredient (TGAI).

i. *Avian dietary toxicity.* In the current regulation, the Agency requires the subacute avian dietary toxicity study (guideline 850.2200) for terrestrial and aquatic (food crop and nonfood), forestry, and domestic outdoor uses, and conditionally requires this study for indoor and greenhouse (food crop and nonfood) use sites, as part of a set of 4 basic avian (acute and dietary) and aquatic toxicity studies. The results are used in decisions regarding environmental hazard statements on product labeling. Since the avian acute oral study more accurately reflects the inherent exposure to birds in this scenario, the Agency is proposing to no

longer require the avian dietary study for indoor and greenhouse uses.

This proposal would also add as a conditional requirement data on one avian species for aquatic nonfood residential uses if the acute avian oral LD_{50} of the TGAI is less than or equal to 100 mg a.i./kg. Data would be required on a second species for this use if the avian dietary lethal concentration to cause mortality in 50% of the test animals (LC_{50}) in the first species tested is less than or equal to 500 ppm a.i. in the diet. The Agency is proposing to conditionally require the second species because the data will provide some assurance that EPA is not basing an assessment on a single species which might be highly sensitive (or the opposite) when compared to other birds. This particular use category (aquatic nonfood residential) is relatively small-scale, so the current regulations require testing on only one species. However, in the event that this test shows high toxicity, this concern is addressed by the conditional requirement for testing on a second species.

ii. *Wild mammal toxicity*. The Agency proposes to amend this conditional data requirement to eliminate the requirement for aquatic nonfood residential uses. In splitting the current aquatic use category, EPA is able to tailor the requirement to those use situations for which the data are needed (aquatic food and nonfood uses). The conditionality of the requirement would be unchanged, that is, required on a case-by-case basis depending on the results of lower toxicology tier studies, such as acute and subacute testing, intended use pattern, and environmental fate characteristics that indicate potential exposure.

iii. *Avian reproduction.* Because some pesticides are stable in the environment, or can be stored in plant tissues that may be used by birds as a food source, avian reproduction testing (guideline 850.2300) is conditionally required for pesticides to which birds are exposed repeatedly or continuously during or preceding the breeding season. In addition, research has shown that even short-term exposures to pesticides can lead to significant adverse reproductive effects. For example, several organophosphorus insecticides have been shown to significantly reduce egg production and lead to changes in eggshell quality within days of dietary exposure (Refs. 4, 5 and 6). Therefore, EPA proposes to require these studies for terrestrial (food crop, feed crop, and nonfood), aquatic food crop and nonfood outdoor, forestry, and residential outdoor uses.

iv. *Simulated or actual field testing for mammals and birds.* Current part 158 conditionally requires field testing (guideline 850.2500) for terrestrial and aquatic (food crop and nonfood), forestry, and domestic outdoor uses. The Agency proposes to expand this conditional requirement to include terrestrial feed crop and aquatic nonfood outdoor uses, as well. The requirement would be based on the results of lower tiered studies such as acute and subacute bird and mammal testing, intended use pattern, and environmental fate characteristics that indicate potential exposure. Testing would be required only for those products that appear to pose significant risks to nontarget wildlife. The Agency is also proposing to require independent laboratory validation of the environmental chemistry methods used to generate data associated with this study.

v. *Acute toxicity: freshwater fish.* Currently part 158 requires the freshwater fish toxicity study (guideline 850.1075) for terrestrial and aquatic (food crop and nonfood), forestry, and domestic outdoor uses and conditionally requires these studies for greenhouse (food crop and nonfood) and indoor uses.

Although indoor and greenhouse uses usually require only one species of fish to be tested, in some instances a second fish species may be needed. For example, a chemical may be shown to be stable in the environment (*i.e.*, hydrolysis study), have moderate toxicity (1 ppm LC_{50} < 10 ppm) in the acute fish toxicity study, and may be released into the aquatic environment through effluent discharge. In such cases, the results of the two required acute aquatic toxicity studies (fish and invertebrates) may not be sufficient to rule out greater toxicity in a second species of fish. Testing on a second species will provide some assurance that EPA is not basing an assessment on a species that is highly sensitive (or the opposite) when compared with another species. Therefore, in these cases, the Agency proposes to conditionally require a third acute study on a second species of fish to correlate with the results of the previous two acute aquatic studies and to ensure that the labeling is adequate to protect aquatic species. The additional study increases the likelihood that effluent criteria and product labeling reflect the pesticide's risk and inherent toxicity.

vi. *Acute toxicity—estuarine and marine organisms.* Acute data from estuarine testing enables the Agency to perform a risk assessment by comparing the toxic concentrations with the estimated or monitored levels in estuaries. The Agency proposes to change the conditional requirement for the acute LC_{50}/EC_{50} testing (guidelines 850.1025, 850.1035, 850.1045, 850.1055, and 850.1075) for terrestrial, aquatic (food crop and nonfood outdoor), residential outdoor, and forestry uses to required testing, and change the aquatic nonfood residential use to ''not required.'' Generally, three out of the five studies would be needed to satisfy the data requirement. Registrants may request a waiver of the study if the crop is never associated with coastal counties or there is a geographical restriction for a site that would normally be of concern.

vii. *Chronic toxicity—fish early-life stage and aquatic invertebrate life-cycle.* Currently, the Agency conditionally requires fish early-life stage and aquatic invertebrate life-cycle studies (guidelines 850.1300, 850.1350, and 850.1400) for terrestrial food and nonfood, aquatic food and nonfood, forestry, and domestic outdoor uses. These studies are not required for greenhouse food and nonfood, and indoor uses. The Agency is proposing several revisions that would clarify the applicability of the requirements. The first is to list the fish early-life stage and aquatic invertebrate life-cycle studies as separate requirements in the data table; then identify each test organism as a freshwater or saltwater species.

For the freshwater fish early-life stage and invertebrate life-cycle studies, the Agency proposes to change the conditional requirement for terrestrial and aquatic (food crop and nonfood) and forestry uses to required, and change the aquatic nonfood residential use to not required.

Currently, the freshwater invertebrate life cycle and fish early life stage tests are conditionally required for terrestrial, aquatic (food crop and nonfood), and forestry uses. When promulgated in 1984, one basis for the conditional nature of the requirements was that only one of the two tests was required, depending on whether fish or invertebrates were more sensitive in the acute studies. However, when a pesticide enters the aquatic environment, both groups of organisms will be exposed. Moreover, acute sensitivity is not a reliable indicator of chronic sensitivity, whether in the same or a different group of organisms, so that chronic data are needed regardless of the results of acute testing.

The proposed change to ''not required'' for aquatic nonfood residential use is due to the fact that the current ''aquatic nonfood'' use pattern is proposed to be split into aquatic

nonfood outdoor and aquatic nonfood residential. As the latter represents a much smaller use pattern, the Agency believes that data requirements can be reduced or eliminated for aquatic nonfood residential uses.

In addition, the Agency proposes to require both of these tests for all turf uses including residential, since exposure varies. This change is warranted because the relative sensitivity of fish and invertebrates can vary widely across chemicals. Currently, only the most sensitive of the two organisms, either fish or aquatic invertebrates, as determined by Tier I acute studies, is tested. However, since both organisms will be exposed when a pesticide enters an aquatic environment and the acute sensitivity of an invertebrate may not accurately predict the chronic sensitivity in fish and vice versa, the Agency believes that both species should be tested for chronic effects. The Agency cannot make the assumption that a chemical is not chronically toxic at much lower concentrations than some ratio of the LC_{50} value would suggest.

viii. *Aquatic organism bioavailability/biomagnification/toxicity tests.* The Agency proposes to eliminate the requirement for these studies for aquatic nonfood residential or residential outdoor uses since exposure is expected to be minimal (*i.e.*, insufficient quantities to accumulate in the tissues of aquatic organisms (guidelines 850.1710, 850.1730, and 850.1850).

ix. *Simulated or actual field testing for aquatic organisms.* The Agency is clarifying that the conditional requirement (guideline 850.1950) applies to turf, however these studies would no longer be required for aquatic nonfood residential uses since exposure is expected to be minimal.

x. *Honeybee acute contact toxicity.* EPA is proposing to require this study (guideline 850.3020) for terrestrial (food crop, feed crop, and nonfood), aquatic food crop and nonfood (outdoor), forestry, and residential outdoor uses. This study is being added to the battery of studies required to support outdoor uses when honeybees are likely to be exposed to pesticides. Previously, the requirement was limited to outdoor use patterns when the crop may be in bloom and thereby be attractive to honey bees. The change from ''conditionally required'' to ''required'' is to address those situations where blooming, pollen-shedding, or nectar-producing parts of nontarget plants adjacent to or within the treated area may be attractive to honey bees. Registrants may request a waiver of the study if use practices significantly restrict exposure of the pesticide to honey bees.

xi. *Honeybee-toxicity of residues on foliage.* The current regulation conditionally requires honeybee toxicity of residues on foliage studies (guideline 850.3030) for terrestrial and aquatic (food crop and nonfood), forestry, and domestic outdoor uses. The study is required when the formulation contains one or more active ingredients having an acute LD_{50} of less than 1 µg/bee. The Agency proposes to amend the requirement to require testing on the TEP when the formulation contains one or more active ingredients having an acute LD_{50} of <11 µg/bee, as determined in the acute contact study, and the use pattern indicates that honey bees may be exposed. The proposed data requirements rule (48 FR 53192) which was published in 1982, listed the correct value of <11 µg/bee for the honeybee study.

xii. *Field testing for pollinators.* The Agency proposes to include terrestrial (feed crop) and aquatic nonfood (aquatic outdoor and residential) uses where honeybees are likely to be exposed to pesticides as a conditional requirement (guideline 850.3040).

C. Data Requirements Specific to Endangered Species Assessments and Determinations

Over the last several years, the Agency has been requiring, on a case-by-case basis for certain pesticides, data demonstrating specific geographic location(s) of threatened and endangered species (listed species), which can then be compared with areas of potential pesticide use. These data have been required when EPA determined that the estimated environmental concentration of the pesticide when applied according to the labeling appears to exceed the Agency's numeric concern levels for listed species. The specific species for which location information was needed, has been determined on a case-by-case basis based upon the use pattern of the pesticide and the sites on which it may be used. These special data are currently not required by part 158, and have only been requested on a few occasions; however, the Agency anticipates that they may be requested in the future in connection with other registration and reregistration actions. In response to a Data Call-In notice for data on the location of all listed species, an industry task force is working to develop a database that may partly fulfill Agency needs, *i.e.*, geographic locations where potentially affected species are thought to occur. Access to the task force data by other registrants who may be required to provide such data in the future would be made available through appropriate data sharing mechanisms. Although the anticipated expanded burden on registrants is not large since it does not entail experimental or laboratory procedures, it is nevertheless not likely to be inconsequential. Consequently, the Agency is requesting comment on its utility and appropriateness.

In addition, through discussions about methods to evaluate the potential risks of pesticides to listed species, EPA and the Fish and Wildlife Service and the National Marine Fisheries Service (jointly referred to as the Services) identified several aspects of EPA's current approach for which there is some scientific uncertainty. While the Services agreed that EPA was using the best available scientific and commercial information to assess risks to listed species, the Services and EPA also agreed that where uncertainties existed, further research and investigation might help to develop improved risk assessment approaches. The Agency recognizes that such research also could lead, in the long run, to additional data requirements for registration. Accordingly, the Agency seeks input on research areas that may be necessary to effectively characterize potential risks to listed endangered species from pesticide use. These include research to address the following types of uncertainties:

- Product use information by geographic location below the state and county levels
- Toxicity data and environmental fate measurements/exposure model predictions with end use products
- Toxicity data from surrogate species that quantify dose-response relationships for effects relevant to critical life stages of endangered species
- Measured or estimated values of physiological, biochemical, and morphological characteristics of endangered species and surrogate species to refine chemical-specific interspecies toxicity extrapolations
- Toxicity, exposure, uptake and elimination data to better determine any differences in interspecies sensitivity of non-target and endangered plant species exposed to herbicides
- Toxicity data to characterize potential effects to freshwater mussels
- Toxicity data to characterize potential effects to reptiles and amphibians.

The Agency seeks comment on:

1. The relative value of each of these research areas in better refining assessments of potential risks to listed species.

2. Input on specific research directions in these areas, including methodologies, protocols etc., that would be appropriate and useful in assessing the potential risks to listed species.

3. Other types of research that would be of value in refining potential risks of a pesticide to a listed species.

4. The extent to which potential research areas reflect uncertainties that apply to pesticides generically; to chemical stressors generically, or to types of pesticides or chemicals stressors.

XI. Toxicology Data Requirements (Subpart F)

A. General

Toxicology studies are required by the Agency to assess the hazard of the pesticide to humans and domestic animals. These hazard data, when combined with exposure data, form the basis for the human risk assessment. Generally, using animals as a surrogate for humans, tests are carried out by the oral, dermal or inhalation route depending on the pesticide's pattern of use and physical form. The duration of the toxicity study approximates the estimated duration of human exposure, while considering species differences in maturational milestones and overall life span. Typical exposures may be ''acute'' (single dose), ''subchronic'' (intermediate), or ''chronic'' (long-term). If a pesticide is used on food and requires a tolerance, the dietary exposure may be over a lifetime, or a significant portion of a lifetime, and thus chronic/cancer and multi-generation reproductive studies would be required. Studies would be required to assess the hazard during a potentially susceptible stage of life, *e.g.*, prenatal developmental studies and developmental neurotoxicity studies, and to measure end points not always observed in the basic toxicity test battery, *e.g.*, acute and subchronic neurotoxicity studies.

In addition, EPA's Risk Assessment Guidelines set forth principles and procedures to guide EPA scientists in the conduct of Agency risk assessments, and to inform Agency decision makers and the public about these procedures. The guidelines emphasize that risk assessments will be conducted on a case-by-case basis, giving full consideration to all relevant scientific information. This case-by-case approach means that Agency experts review the scientific information on each agent and use the most scientifically appropriate interpretation to assess risk. The guidelines also stress that this information will be fully presented in Agency risk assessment documents, and that Agency scientists will identify the strengths and weaknesses of each assessment by describing uncertainties, assumptions, and limitations, as well as the scientific basis and rationale for each assessment.

This proposal includes the requirements for pesticides retained from the current 40 CFR 158.340 as well as proposed revisions that have been peer reviewed by the SAP. The basic data set proposed here includes toxicity studies needed to support high exposure pesticides, such as food use pesticides.

1. Acute studies (oral, dermal, and inhalation toxicity tests, eye and skin irritation tests and dermal sensitization)
2. Subchronic (90–day) feeding studies in rodents and nonrodents
3. Chronic feeding studies in rodents and nonrodents
4. Cancer studies in two species of rodents (rat and mouse preferred)
5. Prenatal developmental toxicity studies in rodents and nonrodents (rat and rabbit preferred)
6. Two-generation reproduction study in rodents (rat preferred)
7. General metabolism study in rodents
8. Mutagenicity battery
9. Acute and subchronic neurotoxicity studies in rats
10. Immunotoxicity study in rodents
11. Developmental neurotoxicity study in rodents

B. Approach

1. *Options for generating data.* A required sequence of toxicological testing for new pesticides is not specified by the Agency. Rather, most decisions regarding the order of testing are left up to the individual registrant, based upon the understanding that there are many factors that could affect the testing progression. It is recommended, however, that the development of pharmacokinetic information, including data relevant to developing systems, be initiated early in the testing process in order to aid in the appropriate design of the studies and the interpretation of toxicological findings in adult and immature (developing) animals.

Generally, data requirements will proceed from single to multiple exposures, from shorter to longer duration, and from simpler to more complex. Different studies may be conducted simultaneously and various studies may be done in combination as well (an approach encouraged by the Agency to optimize resources and reduce the number of animals used in testing). Knowledge gained from results of earlier studies should be used to design subsequent study protocols in order to attain the greatest confidence in the results of the higher-order studies. For instance, conducting the subchronic (90–day) feeding study prior to the two-generation reproduction study would provide information on target organs that may be affected and that need to be specifically evaluated in the two-generation reproduction study.

2. *Options for submitting nonfood use data.* In proposed § 158.510 for nonfood uses of pesticides, EPA proposes to implement two approaches for complying with the toxicology data requirements. The first option, which parallels the testing scheme in the current regulations, would allow registrants and applicants to submit a set of acute, subchronic, chronic, and other toxicological studies on the active ingredient, with the specific makeup of the set of study requirements being based upon anticipated human exposure to the pesticide, as determined by the Agency. The makeup of the set of studies required for non-food use chemicals will be determined by the Agency based on the use pattern and expected exposure scenarios for the chemical. The following two examples illustrate the Agency's approaches:

i. A fairly volatile pesticide is used in the home where long-term exposure by both inhalation and dermal routes are expected. In this case, the toxicity studies required would be similar to that for a food-use chemical.

ii. In another example, a termite control pesticide is buried in the lawn near the house. There is very little exposure to anyone including the applicator. In this case, only Tier 1 data would be needed. In general, the level of toxicity studies will be determined by the magnitude, frequency and duration of the estimated human exposure. If hazards are identified based upon review of these studies, the Agency would decide what types of actual human exposure data (*i.e.*, applicator and post-application studies) also would be required to evaluate risk.

The second option would allow registrants and applicants of nonfood use pesticides to submit both toxicological studies and human exposure data simultaneously. For this option, toxicological data would be submitted under a tiered system. Agency review of the first-tier toxicological studies and the simultaneously submitted exposure data then would determine the need, for second- or third-tier toxicological studies. This option would permit flexibility in study requirements based on the identification and characterization of adverse treatment-

related toxicological effects and dose-response information, and estimates of potential human exposure. Additional second- or third-tier studies would be required on a case-by-case basis.

Under this second option, the required first-tier studies would consist of: Acute studies, a subchronic 90–day dermal study or a subchronic 90–day inhalation study, an acute and subchronic neurotoxicity screening battery in the rat, prenatal developmental toxicity studies in two species, two-generation reproduction study in rodents (rat preferred), immunotoxicity study in rodents, and a full initial battery of mutagenicity studies. The conditionally required second-tier studies would include both subchronic 90–day feeding studies, and sometimes a dermal penetration study. Depending on the results of completed studies, conditionally required third-tier studies would include both Chronic Feeding studies, both carcinogenicity studies, a reproduction study, and a metabolism study. In addition, depending upon the results in the initial neurotoxicity and mutagenicity batteries, further neurotoxicity or mutagenicity testing may be required to address possible identified risk concerns.

C. Proposed Toxicology Data Requirements

EPA's proposed toxicology data requirements encompass studies expected to improve the Agency's understanding of the potential pesticide hazard to humans, including subpopulations such as infants and children. The proposed table in this subpart contains the toxicology data requirements EPA would rely on to identify potential hazards to humans and domestic animals for all conventional pesticides. These include acute, subchronic and chronic toxicity studies, as well as carcinogenicity, prenatal developmental toxicity, reproductive toxicity, mutagenicity, neurotoxicity and other specialized studies.

EPA recognizes that toxicology testing represents a large economic burden on registrants and incorporates the use of test animals. Consequently, the Agency works with industry, the scientific community, and advocates, to ensure that data requirements are imposed only when needed to make a sound scientific safety finding required under the law. Because of this concern, the Agency has adopted guidelines whereby several toxicological endpoints may be derived from one study and has instituted other avenues for combining studies. The Agency also recognizes that, in general, lower exposure uses often correlate with lower risk. Consequently, the Agency has adopted an approach that tends to levy more extensive data requirements on high exposure uses like food uses. It is also reflected in the tiering system for data submissions for nonfood uses and in the layout of the data tables.

1. *Newly imposed data requirements—Immunotoxicity.* The Agency proposes to require immunotoxicity testing for all pesticides. Immunotoxicity testing is necessary to evaluate the potential of a chemical to produce adverse effects on the immune system. Immune system suppression has been associated with increased incidences of infections and neoplasia. In 1993, the National Research Council reviewed the technical literature and found that some pesticides are immunosuppressive (NRC, 1993). Because of the potential for pesticides to adversely impact the immune system, the EPA has developed a test guideline (870.7800) for immunotoxicity. The immunotoxicity test guideline was reviewed and endorsed by the FIFRA Science Advisory Panel and EPA's Science Advisory Board in 1996, and published in 1998 as part of the Office of Prevention, Pesticides and Toxic Substances' harmonized test guidelines.

Because the immune system is highly complex, studies not specifically conducted to assess immunotoxic endpoints are inadequate to characterize a pesticide's potential immunotoxicity, even if some tissues subject to immunotoxic insult are examined. While data from hematology, lymphoid organ weights, and histopathology of routine chronic or subchronic toxicity studies may offer useful information on potential immunotoxic effects, these endpoints alone are insufficient to predict immunotoxicity (Refs. 7 and 8). Therefore, the Agency is proposing to require functional immunotoxicity testing along with the data from endpoints in other studies to predict the potential risk of pesticides on the immune system more accurately. The Agency invites public comment on all aspects of its proposed data requirement for functional immunotoxicity.

2. *Newly codified data requirements—*i. *prenatal developmental toxicity.* The Agency proposes to change the name of this requirement from ''Teratogenicity'' to ''Prenatal Developmental Toxicity'' to correspond with the name of the guideline (870.3700). An information based approach to testing is preferred which utilizes the best available knowledge on the chemical to develop a study protocol and testing strategy. Currently, both studies are required for food use pesticides, but for nonfood uses, only one prenatal developmental toxicity study is required, and the results of that study may trigger the conditional requirement for a second species. However, the response to developmental insult in one species is not necessarily the same in another species. The pharmaceutical thalidomide, which produces severe malformations in rabbits (and humans) but not rats following *in utero* exposure, is a classic example of this species-related difference in response. Additionally, the dose at which maternal or prenatal developmental toxicity is observed may not be the same across species, and the severity of the response in dams or fetuses may also differ. Consequently, there is a concern that the current testing paradigm for non-food use pesticides may not adequately characterize potential hazards to pregnant women and their fetuses. Given that the prenatal developmental toxicity study is used extensively to establish endpoints and doses for acute, short-term, and intermediate-term risk assessment, EPA believes it necessary to require studies in two species for all nonfood pesticides.

The Agency encourages registrants consider the use of combined study protocols in satisfying this requirement. A prenatal developmental toxicity study segment could be added to a two-generation reproduction study in rodents (guideline 870.3800). This can be accomplished by utilizing a second mating of the parental animals of either generation. The dams would undergo cesarean section at one day prior to expected delivery and a separate evaluation would proceed as specified in guideline 870.3700. By combining protocols in this manner, a single study would satisfy the requirement for both prenatal developmental and reproductive toxicity in the rodent. While it is recognized that the cost of the reproduction study would increase somewhat due to the additional work scope, the total cost of the combined study would be substantially less than that incurred by conducting the two studies separately. Moreover, a combined reproduction/developmental protocol would not require the purchase of additional animals, and would increase the efficient utilization of the animals being studied. The second required prenatal developmental toxicity study would then be performed on the rabbit.

ii. *Neurotoxicity.* Neurotoxicity studies evaluate the potential of a substance to adversely affect the structure and function of the adult

nervous system. Since promulgation of the toxicology data requirements in 1984, there has been an increasing concern on the part of the scientific and public health communities that some pesticides may produce functional or structural effects on the nervous system that are not readily observed or adequately characterized in standard toxicological studies. The Agency believes that the current set of neurotoxicity studies are inadequate for some chemicals in their observation of behavioral effects and do not use optimal methods to evaluate the nervous tissue structure and function. To detect and characterize these potential effects more fully in certain chemicals, a battery of more sensitive testing would be required. Several neurotoxicity studies are proposed to be added to the already existing neurotoxicity study requirements for all conventional pesticide registrations. The objective of the new acute and subchronic battery is to evaluate the incidence and severity of the functional and/or behavioral effects, the level of motor activity, and the histopathology of the nervous system following exposure to a pesticide.

A new adult neurotoxicity test battery of seven studies would replace the current adult neurotoxicity test requirements. The current adult neurotoxicity test battery consists of three studies: acute delayed neurotoxicity (hen), 90–day neurotoxicity (hen), and 90–day neurotoxicity (mammal). In the current part 158, an adult acute neurotoxicity study in mammals is not listed. However, an adult subchronic neurotoxicity study is required if the acute oral, dermal, or inhalation toxicity studies show neurotoxicity or neuropathy. Currently, the neurotoxicity studies can be triggered either by statistically and/or biologically significant findings.

Under the proposal, some of these tests would be routinely required and others would be conditionally required. Two studies that would be required are an acute and a subchronic 90–day neurotoxicity study (guideline 870.6200) in rats. The acute study would be required to detect possible effects resulting from a single exposure. The subchronic study is intended to detect possible effects resulting from repeated or longer-term exposures. The requirement for a subchronic neurotoxicity study also may be satisfied by incorporating the required neurotoxicity testing into the standard 90–day subchronic feeding study in rats (guideline 870.3100). The acute and subchronic neurotoxicity studies in adult rats, in addition to providing data on the potential for neurotoxicity, also provide a basis for comparison of the potential for age-related differences in impacts on the nervous system with results from the developmental neurotoxicity study, if needed, for the same chemical.

A new, conditionally required, 28–day delayed neurotoxicity study in hens (guideline 870.6100) would be added. The 28–day delayed neurotoxicity test would be required if results of the acute neurotoxicity study (guideline 870.6100) indicate significant statistical or biological effects, or if other available data indicate the potential for this type of delayed neurotoxicity, as determined by the Agency. The Summary Report of the 1990 OECD Ad Hoc Meeting (Ref. 9) adds:

> In the assessment and evaluation of the toxic characteristics of organophosphorus substances, the determination of the subchronic delayed neurotoxicity may be carried out, usually after initial information on delayed neurotoxicity has been obtained by acute testing or by the demonstration of inhibition and aging of neurotoxic esterase and acetylcholinesterase in hen neural tissue.

The Agency believes that to evaluate the specific type of delayed neurotoxicity associated with some organophosphorus esters and related substances, a subchronic 28–day study in hens, rather than a 90–day study, would provide sufficient data. Thus, the duration of the subchronic hen study has been shortened from 90 days to 28 days. This is based on the finding that test chemicals reach equilibrium from both a pharmacokinetic and pharmacodynamic perpective; that is, the levels that cause effects, *i.e.*, LOAELs and NOELs, would be stable after 28 days of exposure. Another reason is that the 28–day study is able to identify effects as well as the 90–day study in that it includes a requirement for dosing 7 days a week, while the 90–day study only doses 5 days per week, allowing for some intermittent recovery. This change was recommended by a panel of experts at a 1990 OECD ad hoc meeting on various issues in neurotoxicity testing (Ref. 9). Hence, the 90–day study requirement has been deleted from the proposed table. The conditional testing requirement for the acute delayed neurotoxicity study in hens (guideline 870.6100) would be unchanged.

The last three studies that comprise the neurotoxicity test battery are also new data requirements. The scheduled controlled operant behavior, peripheral nerve function, and sensory evoked potential neuropathology studies would be conditionally required if the results of the acute and/or the subchronic neurotoxicity studies show adverse effects on the central nervous system which affect learning, memory or performance, or adverse effects on visual, auditory, or somatosensory senses and/or concerns for peripheral neuropathy. The scheduled controlled operant behavior study (guideline 870.6500) evaluates substances that have been observed to produce neurotoxic signs in other studies (*e.g.*, central nervous system depression or stimulation), as well as substances with a structural similarity to neurotoxicants which affect learning, memory, or performance. The peripheral nerve function study (guideline 870.6850) evaluates substances that have been shown to produce peripheral neuropathy or other neuropathological changes in other studies, as well as substances with a structural similarity to those causing such effects. The sensory evoked potential neurophysiology study (guideline 870.6855) evaluates substances that may affect the visual, auditory, or somatosensory (body sensation) senses. Substances tested include those expected to affect these senses or to detect changes based on data from other studies or based on their structural similarity to substances that do affect these senses. The scheduled controlled operant behavior, peripheral nerve function, and sensory evoked potential neurophysiology studies are being proposed at this time to be conditionally required, subject to the results of acute or subchronic neurotoxicity testing or for other reasons, such as structure activity considerations or to more fully characterize any neurotoxic effects seen in the acute and subchronic studies. The Agency believes that these three studies will be rarely required.

iii. *Developmental neurotoxicity (DNT).* The Agency is proposing that developmental neurotoxicity testing be conditionally required for conventional food use and nonfood use pesticides. In implementing this conditional requirement, registrants are encouraged to apply what is known about the chemical and its toxicity to develop a rational, science-based approach to this testing; this is discussed in more detail below. A DNT would be required (Ref. 10) using a weight-of-the-evidence approach when:

1. The pesticide causes treatment-related neurological effects in adult animal studies, such as:
- Clinical signs of neurotoxicity
- Neuropathology
- Functional or behavioral effects

2. The pesticide causes treatment-related neurological effects in

developing animals, following pre- and/or postnatal exposure such as:

- Nervous system malformations or neuropathy
- Brain weight changes in offspring
- Functional or behavioral changes in the offspring

3. The pesticide elicits a causative association between exposures and adverse neurological effects in human epidemiological studies

4. The pesticide evokes a mechanism that is associated with adverse effects on the development of the nervous system, such as:

- SAR relationship to known neurotoxicants
- Altered neuroreceptor or neurotransmitter responses

In practice, EPA evaluates each pesticide using all available toxicological information that might indicate a need for a developmental neurotoxicity study. The developmental neurotoxicity study (guideline 870.6300) has been requested on a case-by-case basis for certain chemicals for food use and nonfood use registrations since the guideline was finalized in 1991. The Agency is proposing to conditionally require developmental neurotoxicity studies for all neurotoxic pesticides and/or when other criteria are met that indicated a potential for toxicity to the developing nervous system, based upon a weight-of-evidence evaluation of the toxicological database.

The criteria used in this evaluation were developed through extensive scientific peer review, including a 1999 FIFRA SAP expert review (and public comment) on the use of the FQPA 10X factor in pesticide risk assessment (Ref. 11). The Panel concluded that these criteria were reasonable and useful indicators which would increase concern for pre-/postnatal toxicity. EPA proposes the (conditional) addition of the developmental neurotoxicity study to the toxicology testing requirements since the two developmental toxicity studies do not include an in-depth assessment of the development of the nervous system. The SAP acknowledged that the criteria were not adequate for identifying every potential developmental neurotoxicant, supporting the Agency's concern about the criteria's limitations. Accordingly, the SAP agreed with the Agency's approach of calling in the full range of neurotoxicity studies, including developmental neurotoxicity, for existing conventional chemistry food-use pesticides that are known neurotoxicants, and for all new conventional food-use pesticides.

The prenatal developmental toxicity study (guideline 870.3700) and the two-generation reproduction study (guideline 870.3800), evaluate the potential for toxicity to offspring following pre- and/or postnatal exposure to a test substance. The prenatal developmental toxicity study, in which the maternal animals are exposed during pregnancy, is designed to assess fetal growth, viability, and the presence of structural alterations (*i.e.*, variations and malformations that can be detected by careful external, visceral, and skeletal examinations of each fetus). The two-generation reproduction study evaluates fetal and pup growth and development, offspring survival, clinical observations, reproductive system maturation and function, and postmortem findings (*i.e.*, organ weights, macro- and microscopic pathology). The developmental neurotoxicity study is designed to evaluate test animals for functional and behavioral deficiencies, as well as structural alterations to the nervous system, that may result from pesticide exposure that occurs *in utero* and/or during early postnatal life.

Currently, discussions on alternative testing paradigms are underway by the International Life Sciences Institute (ILSI) Health and Environmental Sciences Institute (HESI) under the Agricultural Chemical Safety Assessment Technical Committee. The consensus of this effort to date (ILSI, 2001) (Ref. 12) is that toxicological testing should move away from a rigid guideline-based screening approach and towards a more knowledge-based approach such as is currently used for pharmaceutical testing (*e.g.*, the International Committee on Harmonization, 1994). The Agency is in conceptual agreement with this philosophy and proposes to consider the basic precepts of such a toxicology testing paradigm in the application of the toxicology testing requirements that are used to support pesticide regulatory decisions (*i.e.*, § 158.500).

Under this paradigm, both the selection of studies that would be required, as well as the design of the tests themselves, could be influenced by other substantive and reliable information about the pesticide. Such information could include toxicity and dose-response data from other guideline or non-guideline studies, structure-activity relationships, data on the mechanism or mode of action of the chemical, pharmacokinetic data, studies that examine age-related sensitivity or susceptibility to chemical exposure, and information on potential or actual exposure to humans. These data could be used to inform a more targeted testing approach in the design of studies or to support a position that the requirement for specific toxicology tests listed in part 158 should be waived (under the authority described in § 158.45). For example, on a chemical-by-chemical basis, the design of prenatal developmental toxicity and/or two-generation reproductive toxicity studies (both of which examine toxicological effects on immature animals) could be refined, or alternative tests that examine appropriate functional or structural endpoints would be considered. The proposed HESI approach to testing pesticides is anticipated to be published early summer 2005. Once published, the Agency would consider this approach and make appropriate recommendations following internal and external peer review.

In the case of the developmental neurotoxicity study, a thorough evaluation of all available information, including data on the pharmacokinetics and mode of action of the pesticide (if such data exist), could lead to different conclusions regarding the appropriate way to approach testing. For some chemicals, it might be concluded that adequate testing of the developing nervous system would be best accomplished with a standard developmental neurotoxicity study (guideline 870.6300). Refinements to the guideline study could include, for example, changes to the route and/or duration of exposure (*e.g.*, initiation of dosing to maternal animals prior to gestation day 6, or direct gavage administration to pups during lactation), the evaluation of appropriate biomarkers of exposure or effect, the use of more targeted functional, behavioral, or cognitive testing in offspring, or the histopathological and/or morphometric evaluation of particular regions of the central or peripheral nervous system that are known to be affected by either the chemical or chemical class. For other chemicals, the information in the toxicological data base could lead to the conclusion that an alternative test should be performed instead of a guideline developmental neurotoxicity study, alternative chemical-specific methods could be identified as a preferred option.

In the case of organophosphorus and n-methyl carbamate pesticides whose primary mode of neurotoxic action is inhibition of acetyl cholinesterase, a comparative cholinesterase assay could be conducted in lieu of the DNT given that the inhibition of cholinesterase (ChEI) is the most sensitive effect for these classes of chemicals. Regulation on a threshold (or benchmark) dose for

ChEI should be protective of neurotoxicity. Another example of such a testing scenario would be the use of a comprehensive screen of functional and structural thyroid perturbation (*i.e.*, including T3, T4, and TSH levels) in adult and young animals, for a thyrotoxic chemical that has no other indications of direct nervous system toxicity. In such a case, it can be assumed that identification of maternal or offspring thyroid perturbations would signal any potential alterations in nervous system development, and that minimal effects on the thyroid would be detected at lower dose levels than would result in the types of frank functional, behavioral, or structural alterations that can be detected in the developmental neurotoxicity study. Therefore, it can be presumed that regulation of the chemical on the basis of threshold thyroid effects would be protective of any treatment-related alterations in neurological development that might potentially occur at higher doses. Alternatively, evaluation of the toxicology and exposure data bases for a pesticide may lead to the conclusion that there is no need to conduct a developmental neurotoxicity study, when there is reliable evidence demonstrating the lack of potential for neurotoxicity and/or for human exposure.

Whenever feasible, the Agency encourages registrants to conduct developmental neurotoxicity studies in combination with a two-generation reproduction study. In addition, if preliminary evidence indicates the need for evaluation of structural or functional toxicity of other organ systems in immature animals, these could also be examined within the context of the reproduction study. For developmental neurotoxicity assessment, this can be accomplished, for example, by utilizing the second generation (F_2) offspring that are produced in the reproduction study to conduct the functional, behavioral, and neuropathological testing that is integral to the developmental neurotoxicity protocol. A combined reproduction/developmental neurotoxicity protocol reduces the total number of animals assigned to testing (as compared to the number of animals required when the two studies are conducted independently), and results in a more efficient utilization of the animals already on test. Other benefits of using a combined study approach for any type of targeted functional testing in offspring would include the evaluation of a population of offspring with maximized exposure duration (*i.e.*, that have been treated throughout pre- and postnatal life), greater assurance that steady state levels of test substance in the animals have been achieved prior to testing, and an evaluation of effects within the larger context of assessments of maternal and neonatal toxicity and offspring growth and development. Additionally, combined studies are likely to cost less and take less time, and reduce inter and intra-laboratory variability. The Agency invites public comment on all aspects of its proposed data requirements for developmental neurotoxicity.

iv. *Mutagenicity.* A battery of mutagenic tests is currently required to assess the potential of the test chemical to adversely affect the genetic material in the cell and subsequently serve as part of the Agency's weight-of-the-evidence approach for classifying potential human carcinogens. Mutagenicity data are also used to evaluate potential heritable effects in humans. The Agency is proposing to change the specific types of tests to be performed to satisfy the mutagenicity testing requirement (Refs. 13, 14 and 15). Mutagenicity testing would no longer be subdivided into the categories of gene mutation, structural chromosomal aberrations, and other genotoxic effects, with selection from a wide range of mutagenicity tests allowed to satisfy these categories. A more specific initial battery of mutagenicity tests and relevant information would be required to support the registration of each pesticide product. This initial battery would consist of a bacterial reverse mutation assay with *Salmonella typhimurium* and *Escherichia coli* (guideline 870.5100), an assay with mammalian cells in culture (guideline 870.5300), and an *in vivo* cytogenetics assay (guidelines 870.5385 or 870.5395).

The Agency has selected the bacterial assay because it is a primary test for detecting intrinsic mutagenicity of many classes of biologically active chemicals. The genetics of each test strain of *Salmonella* and select strains of *E coli* have been well-validated and the assay is easy to perform, is used routinely throughout the world, and has an extensive data base of tested chemicals. The mammalian cells in culture assay will detect a wider spectrum of possible genetic endpoints not assayed in the bacterial test. The *in vivo* cytogenetics assay provides an important examination of the potential effect a test compound may have on an intact mammalian system. Data from this study provides information on *in vivo* metabolism, repair capabilities, pharmacokinetic factors (*e.g.*, biological half-life, absorption, distribution, excretion) and target organ/tissue effects.

Since there are many different mutagenicity tests available besides those in the initial battery, other types of testing by the registrant or other investigators may have been performed in the course of product research and development. In addition to the initial battery, data from such mutagenicity tests must be submitted to the Agency, along with a reference list of all studies and papers known to the applicant or registrant concerning the mutagenicity of the test chemical. Having this information at the beginning of a mutagenicity assessment will greatly facilitate EPA's effort to provide a more accurate assessment of the mutagenicity of the pesticide in question.

3. *Revised data requirements*—i. *Acute oral and dermal toxicity.* In addition to performing studies using the TGAI, current requirements give the applicant a choice of performing these studies on the end-use product or a diluted end-use product. However, the Agency has determined that studies using the end-use product (EP) provide the most useful data and would only require additional testing on the diluted form if the product met the conditions for a restricted use classification under § 152.170(b) or special review consideration under § 154.7(a)(1). Hence the Agency proposes to change the test substance to support a registration for an end-use product for these two studies (guidelines 870.1100 and 870.1200) to read ''TGAI, EP, and possibly diluted EP.'' The Agency will notify the applicant when additional testing using the diluted product is required. The Agency invites public comment on all aspects of its proposal to modify the current use of the TGAI to include data from the same tests using the EP and possibly the diluted product.

ii. *Primary eye irritation, primary dermal irritation, and dermal sensitization.* EPA proposes to modify the existing data requirement for the EP to include testing with the TGAI. In order to more fully characterize the toxicity of the active ingredient of a pesticide, tests using the TGAI would now be required in addition to the test performed on the end-use product for these three studies (guidelines 870.2400, 870.2500 and 870.2600) to support the end-use product. Dermal and eye irritation and dermal sensitization testing of the TGAI have not previously been required in the toxicology data requirements table in § 158.340 for the EP. These data, however, serve to identify hazards from exposure to the eyes, skin, and associated mucous membranes to the active ingredient. The

Agency considers this information essential in accurately classifying the eye and skin irritation and the skin sensitization potential of the pesticide, and in determining whether any observed adverse effects are inherent to the active ingredient, or caused by the presence of other ingredients. The Agency invites public comment on all aspects of its proposal to modify the current use of the end-use product to include data from the same tests using the TGAI.

iii. *21–day dermal and 90–day dermal.* For both food and nonfood uses, dermal testing may be needed on the end-use product if the product, or any component in it, could lead to potentially toxic effects or could possibly increase the dermal absorption of the active ingredient. The Agency proposes to require a 21– to 28–day subchronic dermal toxicity test (guideline 870.3200) for all food use pesticides. This test is being changed from conditionally required to routinely required since it is generally needed for worker risk assessments. Analyses of exposure information have shown that this duration of exposure is typical for agricultural workers in various components of their job. Since not all food use applications pose worker risk, the requirement will be tailored to the potential for worker exposure.

Dermal toxicity testing for nonfood uses would be required if the dermal route is the major route of exposure. In this latter case, a 90–day study (guideline 870.3250) is proposed to be required, in lieu of the shorter, subchronic study. This proposed conditional requirement is necessary in order to assess potential hazards associated with dermal exposure. If the major route of exposure for nonfood uses is the dermal route, the 21– to 28–day subchronic dermal toxicity test is insufficient to identify potential hazards.

iv. *Carcinogenicity.* The Agency proposes to change the name of the oncogenicity study to carcinogenicity (guideline 870.4200) to correspond with the name of the guideline. In addition, the Agency has determined that 90–day subchronic range-finding studies generally are needed to select appropriate doses for use in these carcinogenicity studies, since cancer studies with doses that are too low and do not cause any adverse effects can be rejected. These range-finding studies have been performed routinely by most investigators prior to the start of their cancer studies and have been submitted regularly to the Agency for review. Since the carcinogenicity study requires testing on rats and mice (which may differ in their response), the 90–day range-finding studies also need to include both species.

The Agency is proposing to formalize this routine practice by including these studies in the part 158 data requirements. The requirement for the 90–day oral study (guideline 870.3100) will be modified to include ''two rodent species- rat and mouse preferred''. Both rodent species would be required for food use pesticides and conditionally required for nonfood uses.

v. *Reproduction.* Under the current toxicology data requirements, a reproduction study (guideline 870.3800) is required for all food use pesticides, and conditionally required for nonfood use pesticides based on the anticipated level of exposure. The Agency proposes to amend the data table and require a reproduction study for nonfood uses, but qualify the requirement to emphasize that the requirement is based on potential exposure. Data on reproductive effects for a nonfood pesticide would be required unless there is no significant human exposure, as determined by the Agency, in terms of the frequency, magnitude, or duration of the exposure. For example, products such as pesticide treated fabric, diapers, or bedding; insect repellent lotions; or constant-release aerosols for indoor use would require reproductive data. This data requirement is still exposure-based and as such will not always be necessary.

This change is predicated on the fact that reproductive toxicity testing endpoints are not assessed in any of the other required studies for the nonfood uses, and that these other studies do not provide adequate triggers which would indicate the potential for reproductive adverse effects.Multi-generation reproductive studies provide critical scientific information needed to characterize potential hazard to the human population during a number of sensitive life stages, *e.g.*, during *in utero* fetal development, perinatal life, adolescence, and adulthood. These studies can be used to select endpoints and doses for use in risk assessment and are considered a primary data source for reliable reference dose calculations (Ref. 16).

The need for a reproduction study in Tier 1 is bolstered by information developed by the Pest Management Regulatory Agency (PMRA) of Canada. (Ref. 17). In 1997, PMRA provided to the Agency the results of a preliminary study, which retrospectively evaluated reproduction studies as they affected risk assessment needs. The study was presented in the context of antimicrobial pesticides, for which a tiered toxicology testing scheme was being discussed. However, the results apply to similar tiered testing schemes across a broader spectrum of uses, such as what EPA is proposing for nonfood uses.

One aspect of the PMRA study looked to determine whether a reduced Tier 1 set of toxicology studies (consisting of acute toxicity, subchronic toxicity, developmental toxicity, and mutagenicity studies, but not a reproduction study) would adequately identify reproductive endpoints or concerns for risk assessment purposes. PMRA's results are telling with respect to reproductive effects:

- For 67% of the evaluated chemicals (12/18) with reproductive endpoints of concern, the reduced Tier 1 data set would not have predicted reproductive effects identified in a reproduction study
- Reproductive effects were not limited to a particular class of pesticide
- Chemical structure was not useful as a predictive tool (of reproductive effects)
- Mutagenicity studies were not helpful (in predicting reproductive effects)

EPA believes their results support the inclusion of reproduction studies in the Tier 1 nonfood testing regimen.

vi. *Non-rodent chronic studies.* The Agency is considering eliminating the requirement for a 1–year dog study. Under the current toxicology data requirements, a 1–year non-rodent (dog) study (guideline 83–1) is required for all food use pesticides or for nonfood uses if use of the pesticide product is likely to result in repeated human exposure over a significant portion of the human life-span. Evidence in the published literature suggests that the study may not be needed. (Ref. 18) The Agency's impression from its reviews is consistent with the conclusion reached in that study. However, the Agency possesses a large body of dog studies submitted over the last three decades, and believes it appropriate to conduct a comprehensive and systematic analysis of those studies. EPA is in the process of conducting such an analysis and expects to present its preliminary analysis to the SAP in the spring of 2005. At that time, the analysis and other supporting documents would be made available for public review and comment. If this review confirms that the study is no longer needed, the Agency would in the final rule eliminate the requirement for the 1–year dog study. EPA specifically seeks comment on the possibility of eliminating the 1–year dog study.

D. Further Test Guideline Development

The data base to assess pre- and post-natal toxicity varies depending on the nature of the chemical. Some chemicals may need additional data in addition to the core data set for an adequate evaluation of potential hazards. The following studies may be required on a case-by-case basis to support the registration of particular pesticide products and the Agency has begun developing test guidelines for some of these studies. As the Agency's experience with these studies increases and if the studies are imposed more regularly, EPA may propose to include them in future revisions to part 158.

- pharmacokinetics in fetuses and/or young animals
- direct dosing of neonates prior to weaning for exposure through the maternal route
- specialized developmental neurotoxicity of more sensitive sensory and/or cognitive functions
- developmental immunotoxicity
- developmental carcinogenesis
- enhanced evaluation of potential endocrine disruption.

EPA solicits public comment on the Agency's possible request for such data, including the circumstances under which such data should be required.

XII. Nontarget Plant Protection Data Requirements (Subpart J)

A. General

Plant protection studies are used by the Agency to evaluate the potential for adverse pesticidal effects to nontarget terrestrial and aquatic plant species. Nontarget plants include crop plants growing within the target or treated area (such as crop plants which are growing with weeds or plants which are hosts for insects and disease organisms), and those growing outside the target area (adjacent crop plants, endangered plants, and plants that are important to fish and wildlife for food and cover). Data from the plant protection studies will be used to determine if protective measures, such as precautionary labeling, are needed.

Data on plant protection include short-term acute greenhouse and simulated or full field studies arranged in a hierarchy from basic tests to applied field tests. The results of each tier of tests must be evaluated to determine the potential of the pesticide to cause adverse effects, and to determine whether further testing is required. Tier I and II studies are short-term and relatively inexpensive. They are required broadly to assess a pesticide's potential to harm plants in the early stages of plant growth (the first 14 to 21 days). The short-term acute greenhouse studies provide basic toxicity data which are used in a deterministic risk assessment screen. These data are used to establish acute toxicity levels of the pesticide to the test organisms; to compare toxicity information with measured or estimated pesticide residues in the environment in order to assess potential impacts on plants; and to indicate whether further greenhouse and/or field studies are needed.

If additional, more refined, information is needed, Tier III field studies would be triggered. Simulated field and full field studies may be required when basic data and environmental conditions suggest that the risk exceeds the Agency's level of concern for nontarget plants and the information sought is necessary to adequately refine the Agency's assessment of risk. Data from these studies are used to estimate the potential for adverse effects on plant reproduction and survival, taking into account the measured or estimated residues in the environment.

B. Proposed Plant Protection Data Requirements

EPA is not proposing major changes to the plant protection data requirements from those currently listed in part 158. The proposed data requirements are being expanded to include use patterns where the potential for off-target exposure via surface run-off and spray drift are likely, or for uses that may result in discharges to the aquatic environment. The seed germination study would be eliminated.

In addition, the Agency is proposing to require independent laboratory validation of the environmental chemistry methods for terrestrial and aquatic field testing. Other changes include changes in test substance, conditions under which a test is required or in some cases, not required, and clarification of test notes. These changes are not expected to increase the burden of the existing data requirements.

1. *Newly imposed data requirements.* None.

2. *Newly codified data requirements.* None.

3. *Revised data requirements*—i. *Seed germination.* The Agency proposes to eliminate the requirement for the seed germination study (guideline 850.4200). The information from this study would be obtained from the accompanying seedling emergence study (guideline 850.4100) which is currently required.

ii. *Seedling emergence and vegetative vigor.* Currently, Tier I seedling emergence (guideline 850.4100) and vegetative vigor (guideline 850.4150) studies are required for terrestrial and aquatic nonfood and forestry uses. Tier II tests (guidelines 850.4225 and 850.4250) are conditionally required for the same use patterns and are triggered by the results of the Tier I studies. Due to the potential for surface run-off or spray drift, EPA proposes to expand the seedling emergence and vegetative vigor data requirements to terrestrial food and feed crops, aquatic food crops, and residential outdoor uses. These studies would not be required for aquatic residential uses since limited exposure is expected from this use site.

The Agency also proposes that seedling emergence and vegetative vigor studies be conducted using the TEP instead of the currently required TGAI. The TEP that contains the highest percentage of active ingredient, and/or is the most commonly used, would be required. TEP testing eliminates the need for a separate solvent control because the solvent is already contained in the product formulation.

The Agency also proposes that vegetative vigor studies with granular or bait formulations not be required. Since the protocol for this study requires that the pesticide be applied directly to the plant surface, tests using granular or bait formulations would not be practical.

iii. *Aquatic plant growth (algal and aquatic vascular plant toxicity).* Currently the Agency requires Tier I aquatic plant growth studies for terrestrial and aquatic nonfood and forestry uses, and conditionally requires Tier II studies for these same use patterns using five aquatic plant species (*Pseudokershneria subcapitata* (green algae), *Skeletonema costatum* (marine diatom), *Anabaena flos-aquae* (blue-green cyanobacteria), *Navicula sp.* (freshwater diatom), and *Lemna gibba* (floating vascular macrophyte)) (guidelines 850.4400 and 850.5400). Again, due to the potential for off-target exposure via surface run-off and spray drift, the Agency proposes to extend this requirement to terrestrial food and feed crops, aquatic food crop, and residential outdoor uses. Tier II aquatic plant growth studies are proposed to be conditionally required for aquatic nonfood residential uses, using either the TGAI of TEP.

iv. *Terrestrial field and aquatic field.* The Agency is proposing to extend these Tier III conditional requirements (guideline 850.4300 and 850.4450, respectively) from terrestrial and aquatic nonfood and forestry uses to terrestrial food and feed crop, aquatic food crop, and residential outdoor uses when off-target movement appears likely (*e.g.*, use

patterns that readily release the pesticide into the environment). These phytotoxicity data are needed to evaluate the level of pesticide exposure to non-target terrestrial and aquatic plants and to assess the impact of pesticides on endangered and threatened plants. The Agency is also proposing to require independent laboratory validation of the environmental chemistry methods used to generate data associated with these studies. Independent laboratory validation is used to ensure the accuracy and reproducibility of the analytical methods that were used to conduct field studies. For example, independent laboratory validations have been required for food residue methods since 1989. EPA instituted this requirement because analytical protocols were often poorly written and incomplete in terms of the descriptions of all the necessary steps. The Agency scientists spent excessive amounts of time confirming that the methods worked properly and in some cases they could not duplicate the results of the studies. Since the independent laboratory validations have been required, a higher percentage of methods is successfully validated by EPA scientists and less time is required to do so. For laboratory tests, we rely on Good Laboratory Practice Standards (GLP) to assure the quality and integrity of the data submitted to the Agency. Ensuring reproducibility and quality of studies used in EPA's decision-making are also key components of EPA's Information Quality Guidelines.

XIII. Post-application Exposure Data Requirements (Subpart K)

A. General

While toxicology data depict the potential hazard of a pesticide, residue chemistry, applicator and post-application data serve to estimate the potential exposure to the chemical. Residue chemistry data (subpart O) provide EPA with dietary exposure information, applicator (subpart U) and post-application (subpart K) exposure data provide exposure data from other routes, such as dermal, inhalation, and oral.

The post-application data requirements are being revised because the existing data requirements no longer meet the needs of the Agency to protect human health from unreasonable adverse risks in all post-application settings. Data to determine post-application exposure are essential to assess the risk to people resulting from exposure to pesticides after they have been applied. Results from the post-application residue studies assess the presence of pesticide residues, while exposure monitoring data are used to determine the quantity of the pesticide and any of its potentially harmful degradates or metabolites to which people may be exposed. These data, in conjunction with appropriate toxicology information, are used to determine whether post-application risks are of concern at residential and occupational sites, and to develop, when appropriate, post-application restrictions.

The 1984 data requirements were developed to assess the risks to agricultural workers and others who must enter a treated field. The data were, and still are, required to protect these workers from exposures resulting from pesticide residues remaining on crops. Over the years, occupational safety concerns have led to the development of a number of state and federal programs for agricultural worker protection. More recently, the Agency has become increasingly concerned about post-application risks to persons in occupational settings other than conventional food, feed and fiber crop agriculture. Additional studies and information are needed to assess the risks to workers in nurseries and greenhouses, forests, golf courses, animal facilities, and other settings where a person may be exposed to pesticides. Depending on the setting and the type of application, exposure can result from residues on foliage (including turf grass), soil, or indoor surfaces.

The proposed data requirements also are being expanded to encompass potential risks from other settings where people may be exposed, such as golf courses, recreation areas, schools, and hospitals, regardless of whether they are on the job or are simple bystanders. The Agency has long been aware of the need for exposure data in this area. Under current practice, post-application exposure data are generally required for both occupational and residential settings. Currently, post-application exposure studies are required on a case-by-case basis when specific exposure and toxicity criteria triggers have been met. Moreover, FFDCA now mandates that EPA perform additional scientific analyses which have not been a routine part of the Agency's risk assessment process, such as the assessment of aggregate exposures from multiple pathways including dietary and non-dietary routes. Such exposures to pesticides have been associated with a significant proportion of reported incidents in the record.

Residential use sites, for data requirement purposes, encompass more than what would normally be considered homeowner use. A ''resident'' is a member of the general public, and ''exposure'' from a residential use site includes post-application exposure to anyone who, in the course of their daily activities, comes in contact with a pesticide after it has been applied. Post-application residential exposure to pesticides can occur in a variety of indoor and outdoor environments, and a vast number of different human activities can occur at these sites after the pesticides has been applied. Data reflecting new exposure patterns are required to determine whether a product may be used safely in and around homes, golf courses, parks, recreation areas, schools, hospitals, and public buildings. Numerous pesticides contribute to outdoor residential exposure including lawn chemicals, landscaping and garden products, rodent poison, and treated lumber. Indoor exposures can result from ant and roach killers, termite treatments, pet flea and tick products, and treated paint. While use of some products may result in intermittent exposures, use of others can result in people's exposure to the pesticide or its residues on a daily basis. In addition to acute or episodic exposures, chronic exposure to pesticides used in residential settings may be of concern.

EPA's current post-application exposure data base is not comprehensive, especially regarding exposures to pesticides in nonagricultural settings. The new data that would be collected under the approach outlined in this proposal would allow the Agency to conduct improved exposure assessments for residential and occupational sites. In addition, such post-application studies would allow the Agency to assess aggregated and cumulative risks to consumers, with special emphasis on children. The Agency invites public comment on all aspects of its proposed data requirements for post-application exposure.

B. Criteria for Testing

EPA proposes to revise the toxicity and exposure criteria for post-application exposure studies. The Agency currently requires pesticide post-application exposure data when it determines that risks resulting from post-application exposures may be a concern in occupational or residential settings. The criteria for requiring post-application exposure monitoring data would be expanded to include a wider number of potential exposure scenarios in both occupational and non-occupational settings. The

determination of whether or not a pesticide meets these criteria would be made by the Agency on a case-by-case basis.

1. *Toxicity criteria.* In the 1984 regulations, EPA required post-application exposure data if the pesticide was classified as category I for acute dermal toxicity. EPA, however, is proposing to modify the toxicity criteria for requiring post-application exposure data. While the Agency remains concerned about pesticides that are highly toxic by the dermal route or that cause other significant effects by the dermal route, there is also strong concern about other types of toxic effects such as neurotoxicity, developmental effects and general systemic effects which are seen in oral studies, but would be relevant to any risk related to post-application exposure.

EPA is proposing that the toxicity criteria be based on all aspects of the toxicity of the active ingredient. Post-application exposure data would be required, as determined by the Agency, if the active ingredient meets any of the following including:

- Evidence of potentially significant adverse effects have been observed in applicable toxicity studies,
- Scientifically sound epidemiological or poisoning incident data indicate that adverse health effects may have resulted from post-application exposure to the pesticide.

2. *Exposure criteria.* EPA proposes to expand the exposure criteria that would trigger post-application exposure studies to include residential settings and certain occupational settings both indoors and outdoors. Specifically, EPA is proposing the following exposure criteria. When there is potential exposure to humans from post-application pesticide residues from any media, typically, these exposures fall into the following areas.

i. *For outdoor uses:*

- Occupational human post-application exposure to pesticide residues on plants or in soil could occur as the result of cultivation, pruning, harvesting, mowing or other work related activity. Such plants include agricultural food, feed, and fiber commodities, forest trees, horticultural plants in commercial greenhouses or nurseries, and turf grass,
- Residential human post-application exposure to pesticide residues on plants or in soil could occur. Such plants include turf grass, fruits, vegetables, and ornamentals grown at sites, including, but not limited to, homes, parks, and recreation areas.

ii. *For indoor uses*:

- Occupational human post-application exposure to pesticide residues could occur following the application of the pesticide to indoor spaces or surfaces at agricultural or commercial sites, such as, but not limited to, agricultural animal facilities and industrial or manufacturing facilities,
- Residential human post-application exposure to pesticide residues could occur following the application of the pesticide to indoor spaces or surfaces at residential sites, such as, but not limited to, inside homes, daycare centers, hospitals, schools, and other public buildings.

The need for data from potential exposure resulting from situations not covered by these examples should be discussed with the Agency.

C. Proposed Post-application Exposure Data Requirements

At a minimum, residue dissipation, exposure studies, and selected toxicity data are needed to assess post-application risk and determine, when appropriate, entry restrictions. Product use information, including registrant-generated or other surveys on actual use, and descriptions of human activity information are also used to define and refine post-application exposure and risk estimates.

The dissipation of pesticide residues may occur on foliage, soil, or indoor surfaces. To determine dissipation rate, the Agency uses, depending on the use of the pesticide, dislodgeable foliar residue dissipation data, turf grass transferable residue dissipation data, soil residue dissipation data, and/or indoor surface residue dissipation data. To determine the level of post-application human exposure, EPA may use dermal exposure, inhalation exposure, and/or nondietary ingestion studies. In some instances, such as exposure to swimmers, where passive dosimetry methods are not feasible, EPA may require a biological monitoring study. The Agency does not believe that this study will be commonly required. Certain toxicity data also are used in conjunction with the dissipation and exposure data. Typically, this information is obtained through existing toxicity data requirements (see Unit XI of this preamble and subpart F in the proposed regulatory text).

Post-application exposure monitoring data are proposed to be pesticide- or formulation-specific, however, surrogate exposure data may be submitted, if appropriate. In general, the studies required for estimating post-application exposure are dependent upon the pesticide site and use patterns, potentially exposed populations, significant exposure routes, and the time duration over which the exposure occurs. The employment of exposure mitigating measures, such as packaging or use restrictions, *e.g.*, tamper-resistant bait stations, may alleviate the need for some or all of the data requirements in subpart K. Data would be required when any of the testing criteria is met. The Agency does not believe that ''full'' studies will be commonly required. Applicants are strongly encouraged to consult with the Agency to determine specific data requirements for their product.

1. *Newly imposed data requirements.* None.

2. *Newly codified data requirements.* EPA is proposing to base its data requirements for post-application exposure information on two distinct use patterns: occupational and residential. In doing so, the Agency proposes to expand the data requirements for post-application exposure data to include residential sites, nonagricultural sites, and agricultural sites other than conventional food, feed and fiber crop agriculture, which would include greenhouses, nurseries, forests, and animal facilities. New data requirements include indoor surface residue dissipation, biological monitoring data, product use and human activity information, nondietary ingestion exposure, and data reporting and calculation methodologies.

i. *Indoor surface residue dissipation.* The Agency proposes to add the Indoor Surface Residue Dissipation study (guideline 875.2300) as a new post–application exposure data requirement. These data characterize the pesticide residues found inside buildings on surfaces such as flooring, carpets, upholstery, counter tops, and other treated surfaces after the pesticide has been used. The measurement of indoor pesticide residues is particularly important for characterizing exposure to subpopulations that may spend a large portion of their time indoors, such as children or the elderly. Such data will be used to determine whether or not a pesticide could be safely used in an indoor residential or occupational setting.

ii. *Biological monitoring.* Biological monitoring data (guideline 875.2600) measure the amount of chemical to which a person has been internally exposed. This is done by measuring pesticide and/or metabolite compound concentrations in selected human tissues, fluids, or bodily wastes (feces and/or urine). EPA proposes to conditionally require biological

monitoring studies as an alternative to passive dosimetry techniques. The Agency is providing this alternative because, typically, an exposure assessment will be performed relying on generic passive dosimetry data, which measures the potential dose or amount of the chemical on skin or in the air. However, passive dosimetry data usually overestimate exposure, because they only provide estimates of potential exposure, not measurements of absorbed dose. A biological monitoring study performed under the same label use conditions as the passive dosimetry study will provide data on the actual absorbed dose and will result in more accurate and refined risk assessments. Often, biological monitoring studies are voluntarily submitted by registrants. Again, both passive dosimetry studies and biological monitoring studies are always performed under real-world conditions and are representative of actual post application activities.

In addition, the Agency proposes to allow registrants to submit biological monitoring data in addition to, or in lieu of, dermal or inhalation passive dosimetry data provided adequate pharmacokinetic data are available and sufficiently understood to interpret the results.

iii. *Product use information.* EPA is proposing to require product use information (guideline 870.2700) for both the occupational and residential use patterns. Product use information will provide EPA with information about how the pesticide is actually used and applied. Data will include major use sites, typical application methods, ranges and typical values for application rates, timing and number of applications per season or per year, geographical distribution of use, use surveys, post-application entry restrictions, restricted-entry intervals, any available surveys that provide use information, and other use information relevant to potential exposure following a pesticide application. This use information will enable the Agency to conduct more accurate and realistic risk assessments, thus enabling the Agency to levy appropriate limitations on use to mitigate potential risks.

iv. *Description of human activity.* In addition to use information, the Agency proposes a new requirement describing the possible activities (guideline 875.2800) in which people may be engaged after a site has been treated. Human activities play a crucial role in the nature and magnitude of exposure to pesticides. These data are also useful for evaluating potential differences in exposures between different subpopulations (*i.e.*, adults and children), and for determining how specific activity patterns affect exposure levels. Data would include information on types of human activities associated with use of the pesticide, principal source(s) of exposure, conditions (if any) mitigating exposure, expected frequency and duration of activities (including hours per day and days per year), description of exposed population, typical clothing worn and equipment used, any available surveys that provide human activity information, and other relevant use data.

In many cases, product use information coupled with the description of human activity information are used to help the Agency determine the most likely route(s) of exposure, whether through the skin, through the lungs, or through incidental ingestion.

v. *Data reporting and calculations information.* EPA proposes to require registrants to submit data reporting and calculation information whenever post-application exposure data are submitted. Data reporting and calculations information (guideline 875.2900) is an important component needed to assess the validity of the studies and the accuracy of the exposure calculations. Minimal information that must be submitted includes a description of the purpose of the study and what requirement(s) it is intended to satisfy, a summary of the study, a comprehensive section on materials, methods, and calculations, a section interpreting the scientific results of the study, a discussion of quality assurance, identification of the location of the raw data, and any relevant references, communications, and protocols.

vi. *Nondietary ingestion exposure.* The Agency proposes to conditionally require a nondietary ingestion exposure study (guideline 875.3000) to evaluate the potential oral exposures to humans, particularly children, from pesticide residues from sources other than food. Nondietary ingestion exposure would be expected in residential settings following applications such as:

(1) lawns (soil that contains pesticide residues);

(2) residential plantings (pesticide-treated foliage);

(3) outdoor surfaces (decks);

(4) indoor surfaces (pesticide-treated paint chips);

(5) residential fabrics (clothing, bedding, carpets);

(6) insect and rodent baits.

Nondietary ingestion may also occur through hand-to-mouth orobject-to-mouth transfer of pesticide residues during activities performedby children (e.g., crawling) that put them in close proximity with treatedsurfaces.

Studies would address such concerns as examining behavior patterns,monitoring the amount of soil or residue in the rinsate from hand-washing,and developing science-based models or formulas to estimate theinadvertent exposure. The results from these studies will be used toassess the risks associated with the incidental ingestion of pesticides bychildren following pesticide applications in residential settings. TheAgency is primarily concerned with nondietary exposures immediatelyfollowing application of the pesticide, therefore dissipation studiesalone would not provide the information needed to assess risks fromnondietary ingestion exposures. This study would not be required foroccupational uses.

3. *Revised data requirements.* In addition to newly codified test requirements, EPA proposes to make significant changes to the existing post-application exposure data requirements. The use patterns requiring testing would be expanded from conventional food, feed, and fiber crop agricultural use sites to include other use sites as well. In some cases, the test requirement would change from ''conditionally required'' to ''required,'' and/or the test notes have been reworded to be clearer and easier to understand.

i. *Dislodgeable foliar residue dissipation and turf transferable residues.* The Dislodgeable Foliar Residue Dissipation study (guideline 875.2100) is currently conditionally required for evaluation of post-application conventional food, feed, and fiber crop agricultural exposure. The Agency proposes to expand this requirement to include testing for greenhouse, nursery, forest, and residential settings and change it from ''conditionally required'' to ''required'' for all use patterns. Applicants are encouraged to consult with the Agency to determine their applicable data needs. Like dislodgeable foliar residues, turf grass transferable residues are the amount of pesticide residues deposited onto the leaf surface that have not been absorbed into the leaf or dissipated from the surface, and that can be dislodged from the leaf surface. Turf grass transferable residues are pesticide residues on the surfaces of treated lawns, sod farms, golf courses, or other turf grass that are available for transfer to exposed humans (*e.g.*, golf course workers and golfers, adults and children at residences, reentry workers on sod farms) when they contact the treated turf surfaces. These additional tests are necessary to evaluate dermal exposures

resulting from contact with pesticide-treated plant surfaces, whether residential or occupational.

ii. *Soil residue dissipation.* The Agency proposes to also expand the Soil Residue Dissipation study (guideline 875.2200) to include broader agricultural (greenhouse, nursery, forest) and residential settings. This study would be required for occupational use sites and conditionally required for residential use sites. Soil residue dissipation data are used with toxicological endpoints of concern and concurrent human dermal exposure monitoring data to produce quantitative post-application risk assessments and to determine whether post-application risks from contact with treated soil are of concern at residential and occupational sites. TBTH and methyl parathion for use in nut tree plantations are examples of situations in which EPA found that these were exposures of concern. Without this data, the Agency would not be able to estimate exposure in these scenarios.

iii. *Dermal and inhalation exposure.* The Agency proposes to expand the data requirements for Dermal and Inhalation Exposure studies (guidelines 875.2400 and 875.2500) to include post-application exposure in occupational and residential (indoor and outdoor) settings. Both studies would be required instead of conditionally required for all use patterns. Currently, EPA requires dermal post-application exposure data when agricultural workers are expected to have contact with pesticide-treated food, feed, or fiber crops growing outdoors. The Agency proposes to expand the data requirements to include persons exposed to pesticide residues in residential settings and in other occupational settings, such as greenhouses, nurseries, forests, golf courses, and certain indoor environments. The Agency needs post-application dermal and inhalation data in order to perform the residential risk assessments needed to fulfill the requirements of the Food Quality Protection Act. In addition, the original requirements were not broad enough to assess risks to occupational workers in greenhouses, nurseries, forests, golf courses, and certain indoor environments, where post-application exposures may be a concern. The Agency has imposed two major DCI's for dermal and inhalation exposure data for agricultural chemicals (*e.g.*, diazinon, iprodione, and chlorsulfuron) and for those applied to lawns (*e.g.*, MCPA, triadimefon, trichlorfon, isofenphos, and cyfluthrin).

4. *Use of surrogate data.* Surrogate data are data collected for another pesticide that may be applicable to the pesticide under review. Surrogate post-application exposure data are data generated using comparable methods and under similar conditions, and where contact with the treated surfaces is likewise similar. The assumption in the use of surrogate data is that in many post-application scenarios, the physical parameters of the contact with residues on varying surfaces (*e.g.*, foliage, turf grass, soil, indoor surfaces), not the chemical properties of the pesticide itself, are most important in determining the level of residue transfer from treated surfaces to people.

At this time, EPA generally is not allowing the use of surrogate data for any of the post-application residue data (guidelines 875.2100, 875.2200, 875.2300, and 875.3000). EPA encourages applicants and registrants to generate needed exposure data using the pesticide product for which the registration is sought. Surrogate data are, however, accepted under certain circumstances for post-application exposure monitoring. The Agency recognizes the need to impose exposure data requirements judiciously to avoid unnecessary economic burdens on applicants. Surrogate exposure data estimations must have adequate information to address post- application exposure data requirements and must contain adequate replicates of acceptable quality data to reflect the exposure of concern, such as the type of plant or indoor surface and the post-application activity. When the data meet these criteria, the residue transfer coefficients derived from surrogate studies may be used to assess the occupational and residential post-application exposure to the pesticide. When surrogate data, however, prove inadequate for the Agency to estimate likely exposures, applicants and registrants will be required to submit the data required in subpart K.

Surrogate data may be obtained from several reliable sources. Some surrogate post-application data for workers in agricultural settings is available through the Agricultural Reentry Task Force. The task force has submitted to the Agency post-application exposure data. A database was developed that contains transfer coefficients for various agricultural work tasks and crops. Some surrogate post-application data for pesticide applications in residential settings is available through the Outdoor Residential Exposure Task Force. This task force submitted data to the Agency on post-application exposures following the use of different types of pesticide formulations typically found in outdoor residential settings.

In addition, the Agency may accept surrogate exposure data estimations from other agencies, such as the National Institute of Occupational Safety and Health (NIOSH), the Occupational Safety and Health Administration (OSHA), or the OECD to satisfy post-application exposure data requirements, if the data meet the basic quality assurance, quality control, good laboratory practice, and other scientific requirements set by EPA. Moreover, if EPA determines that industrial standards, such as the workplace standards set by OSHA, provide adequate protection for a particular pesticide use pattern exposure, data may not be required for that use pattern. The Agency invites public comment on all aspects of its proposal regarding the use of surrogate exposure data.

XIV. Environmental Fate Data Requirements (Subpart N)

A. General

Under current part 158, EPA requires a series of individual laboratory studies as well as field studies to assess the behavior and fate of a pesticide in the environment. Controlled environmental fate and transport laboratory studies are used to determine the persistence, mobility, and bioconcentration potential of a pesticide active ingredient and its major degradates. The studies offer information on how, or by what mechanism, the pesticide degrades or dissipates, the rate at which it degradates or dissipates, where it goes, and what transformation products are formed. Data from these studies are used as inputs to exposure models. These models estimate the expected environmental concentrations of the pesticide and its degradates under various environmental and use conditions. The laboratory studies also help to focus field study design by providing information on which transformation products are likely to be produced, and thus need to be tracked, and the environmental media (*e.g.*, soil, sediment, water, air) that should be sampled, including the depth to which soil/sediment samples should be collected.

A conceptual model (hypothesis) is developed using assumptions derived from the laboratory data. Since the laboratory studies are controlled and evaluate specific fate and transport properties individually (*i.e.*, degradation, metabolism, mobility, and bioconcentration), they allow for the development of a conceptual model that includes only those fate processes and degradates that are ''significant'' to the pesticide in question. Although

laboratory data are the foundation for the hypothesis and the basis for the conceptual model approach, field studies provide the primary mechanism for testing and refining the hypothesis for the environmental fate and transport of a pesticide. Field studies give site-specific information on the fate and transport of a pesticide and its degradates under actual use conditions.

The field and laboratory data are integrated to characterize the persistence and transport of the pesticide and its degradates in the environment. From these data, quantitative environmental fate and drinking water exposure assessments are developed. Model-estimated environmental concentrations of the pesticide in different media under various pesticide application and site scenarios are calculated. These estimates of exposure are used in conjunction with toxicity data to assess whether a pesticide has the potential to cause adverse effects on human health and the environment, such as, wildlife, fish, and plants, including endangered species.

Persistence studies assess what happens to a pesticide when it interacts with water, soil, air, and sunlight. Mobility studies attempt to predict the potential of the pesticide to volatilize into the atmosphere, move into ground or surface waters, or bind to soil. Bioconcentration studies evaluate the potential to partition to aquatic biota and the degree to which bioconcentration can be reversed should external exposure to the active ingredient or degradates be reduced or eliminated. These studies are designed to help characterize how a pesticide active ingredient dissipates once it is released into the environment and to identify the major degradates that may result from these processes.

Degradation studies include hydrolysis, photodegradation in water, photodegradation in air, and photodegradation on soil. The hydrolysis study determines the potential of the pesticide to degrade from the influence of water alone. Photodegradation studies determine the potential to degrade in water, soil, or air when exposed to sunlight. During these studies, data are also collected concerning the identity, formation and persistence of major degradates.

Metabolism studies include aerobic soil metabolism, anaerobic soil metabolism, anaerobic aquatic metabolism, and aerobic aquatic metabolism. The soil microbial metabolism studies determine the persistence of the pesticide when it interacts with soil microorganisms under aerobic and anaerobic conditions. The aquatic metabolism studies produce similar data, but are generated by pesticide interaction with microorganisms in a water/sediment system. These studies also identify the significant degradates that result from biological degradation.

Mobility studies, which include leaching, adsorption/desorption, and volatility, provide information on the mode of transport and eventual destination of the pesticide in the environment. Scientists can predict the degree of pesticide mobility in soil from data generated from leaching and adsorption/desorption studies.

Bioconcentration studies in aquatic organisms are used to estimate the potential of a pesticide, under controlled laboratory conditions, to partition to the organisms from respiratory and dermal exposures. These studies also provide information on the degree to which bioconcentration of a pesticide or degradate can be reversed should pesticide levels in the surrounding aquatic environment be reduced.

Field studies which identify the environmental dissipation processes, assess the transformation, transport, and fate of a pesticide under actual use conditions with typically applied pesticide product at representative field sites. These studies characterize the relative importance of each route of dissipation of the pesticide and its major degradates. Data generated from field dissipation studies can provide more realistic estimates (albeit limited in time and space) of the persistence and transport of an active ingredient and its degradates when the pesticide product is applied under actual use conditions.

B. Proposed Environmental Fate Data Requirements

The Agency is proposing to revise the environmental fate data requirements. The Agency is proposing to expand the applicable use pattern for the aerobic soil metabolism, terrestrial field dissipation, and aquatic field dissipation studies. The ground water monitoring study would be added as a separate requirement in the table.

The Agency is also proposing to require independent laboratory validation of the environmental chemistry methods used to generate data associated with the dissipation studies. Two residue studies, confined and field rotational crops, would be moved to the residue chemistry data requirements (subpart O). The long-term soil field dissipation study would be merged with the terrestrial field dissipation study. The accumulation study in irrigated crops would be eliminated. Other changes include conditions under which the tests are required or in some circumstances not required, and clarification of test notes.

1. *Newly imposed data requirements--aerobic soil metabolism.* The Agency is proposing to conditionally require this test (guideline 835.4100) for aquatic food crop and aquatic nonfood uses in cases where the pesticide is applied to aquatic sites that are intermittently dry. Such sites include, but are not limited to cranberry bogs and rice paddies. EPA is proposing this change because pesticides which are applied to these sites are more likely to follow degradative pathways that resemble terrestrial rather than aquatic systems. This change was presented to the SAP in 1994, which endorsed the change.

2. *Newly codified data requirements*—i.*Terrestrial field dissipation.* The Agency is clarifying that this requirement (guideline 835.6100) also applies to terrestrial feed crop uses, and is proposing to conditionally require this study for aquatic uses involving application to aquatic sites that are intermittently dry. Such sites include, but are not limited to cranberry bogs and rice paddies. This change was endorsed by the SAP in 1994. While the laboratory studies are designed to address one dissipation process at a time, terrestrial field dissipation studies address pesticide loss as a combined result of chemical and biological processes (*e.g.*, hydrolysis, photolysis, microbial transformation) and physical migration (*e.g.*, volatilization, leaching, plant uptake). Pesticide dissipation may proceed at different rates under field conditions and may result in formation of degradates at levels different from those observed in laboratory studies. Data from these studies can reduce potential overestimation of exposure and risk and can confirm assumptions of low levels of toxic degradates. Results can be used to propose scenario-specific effective risk mitigation. The Agency also proposes to merge this requirement with the long-term field dissipation study (formerly guideline 164–5). The current regulations specify that the long-term field dissipation study is required for pesticides that do not readily dissipate in soil. The field dissipation study would be extended in duration for pesticides that are persistent so that the decline curves for the parent chemical and important degradates can be fully characterized. Since the expanded applicability only applies to uses where the cultural practice of the crop includes periods where the soil is deliberately kept covered with water

then dried, such as in rice or cranberries, the frequency of requesting this study will be quite low. The Agency is also proposing to require independent laboratory validation of environmental chemistry methods for this study to ensure the accuracy and reproducibility of the data, as previously discussed.

ii. *Aquatic field dissipation.* EPA proposes to conditionally require the aquatic field dissipation study (guideline 835.6200) for terrestrial food crop, feed crop, and nonfood uses. The conditions for requiring the study would be:

a. high persistence;

b. high mobility;

c. high potential to bioaccumulate;

d. high acute toxicity to aquatic organisms;

e. high potential for aquatic exposure. Factors such as environmental fate properties, target crops and application methods which are taken into account when determining if the potential for aquatic exposure is high. For example, a persistent and mobile pesticide that is aerially applied is more likely to runoff, drift, and persist in surface water compared to one that degrades rapidly by hydrolysis and is soil incorporated. Since the expanded applicability only applies to uses where the cultural practice of the crop includes periods where the soil is deliberately kept covered with water then dried, such as in rice or cranberries, the frequency of requesting this study will be quite low. The Agency also proposes to require independent laboratory validation for test methods used to generate data associated with this study to ensure the accuracy and reproducibility of the data, as previously discussed.

iii. *Ground water monitoring.* Ground water monitoring studies are designed to determine or confirm the potential of a pesticide or its degradates to reach ground water. The Agency proposes to add a ground water monitoring study (guideline 835.7100) as a conditional requirement for all of the terrestrial uses and for forestry uses. The requirement for ground water monitoring is conditional upon consideration of the toxicological characteristics of the pesticides and its potential to leach into ground water. This study would be triggered if the weight of the evidence of available data indicates that the pesticide and/or its degradates may leach into ground water. Ground water monitoring data may also be requested by the Agency if the existing data base is found to be inadequate to support decisions that are protective of ground water resources.

The likelihood of a pesticide to leach to ground water is initially evaluated by considering the persistence and mobility of the chemical indicated in environmental fate laboratory studies and the field dissipation study required under part 158, and through use of a screening-level simulation model. When the potential for environmental risk is indicated, or cannot be evaluated definitively by this screening assessment, monitoring is used to evaluate the potential of a pesticide to contaminate ground water resources. The results of prospective ground water monitoring studies can provide evidence not available from laboratory studies that natural factors cause a pesticide to degrade without contamination of water resources. Alternatively, they can provide evidence to indicate that ground water contamination could result from use according to the pesticide label, and they can help to quantify the levels at which that can occur.

In providing answers about the potential of a pesticide to leach into ground water and the magnitude of contamination under the most environmentally vulnerable and typical use conditions, ground water monitoring data give risk managers the information they need to make appropriate regulatory decisions. Measured concentrations of pesticides in ground water from prospective ground water monitoring studies are used as screening estimates of potential drinking water exposure for human dietary risk assessments. These studies are also often the best tool with which to estimate pesticide concentrations in drinking water drawn from shallow private wells. Monitoring of private drinking water wells is not required under the Safe Drinking Water Act, and data are therefore scarce for most pesticides.

Under certain circumstances, the Agency also requires ground water monitoring in specified use areas in order to investigate the extent of ground water contamination from previous pesticide use. The use-specific and soil-specific data from field scale monitoring studies also are intended to provide verification for estimates from modeling used to predict the impact of long-term pesticide use on water quality in other use areas. The results of prospective ground water monitoring studies have been and will be used to develop and improve models which allow the Agency to better evaluate the leaching potential of pesticides when data are scarce.

If a pesticide is determined to have a strong potential to leach into ground water and in doing so, poses a risk to human health or the environment, the Agency intends to work with industry to develop the appropriate risk reduction and mitigation measures. Thus, in some cases, ground water monitoring would be required to confirm the effectiveness of these mitigation actions or any other regulatory measures and to elicit appropriate regulatory responses that effectively prevent pollution of ground water resources. The Agency believes that this study will be rarely required.

The Agency is also proposing to require independent laboratory validation of the environmental chemistry methods used to generate data associated with this study. As previously discussed, this evaluation will be used by the Agency reviewers to verify the results of the data submitted.

3. *Revised data requirements—i. Hydrolysis.* EPA proposes to clarify that the requirement for this study applies to terrestrial feed crop and aquatic residential uses. In addition, EPA would conditionally require hydrolysis testing for indoor food and nonfood uses. Hydrolysis testing (guideline 835.2120) may be required to support products for indoor food and nonfood uses for which environmental exposure is likely. Such use sites include, but are not limited to, agricultural premises, in or around farm buildings, barnyards, beehives, and fish or seafood processing premises. The proposed changes reflect concern about the potential movement of pesticides and their degradates into the environment.

ii. *Photodegradation in water.* The Agency is clarifying the applicability of the photodegradation in water study (guideline 835.2240) to reduce the frequency of the requirement, based upon the UV/visible absorption spectrum data submitted as part of the product chemistry data. (§ 158.310) The Agency proposes to indicate in a test note that data on photodegradation in water would not be required in cases where the electronic absorption spectra, measured at pHs 5, 7, and 9 of the chemical and its hydrolysis products, if any, do not show absorption or tailing between 290 and 800 nanometers. These testing parameters were announced in an Environmental Fate and Effects Division Policy Note in March 1992, as well as the 1993 Pesticide Reregistration Rejection Rate Analysis - Environmental Fate (EPA 738–R–93–010).

iii. *Photodegradation on soil.* Currently, photodegradation on soil studies (guideline 835.2410) are conditionally required for terrestrial food crop and forestry uses, with the test note indicating that studies are not required if the use involves application to soils solely by injection of the product into the soil or by incorporation

of the product into the soil upon application. The Agency is proposing to change the designation of the requirement for this study from conditionally required for terrestrial food crop and forestry uses to required, expand the use patterns to include terrestrial nonfood uses, and retain the test note indicating when the studies will not be required. This change represents current practice and is in accord with international harmonization efforts under NAFTA.

iv. *Photodegradation in air.* Data from photodegradation in air studies (guideline 835.2370) provide information about the potential of the pesticide to degrade in air when it interacts with sunlight. Because of the potential for exposure to highly volatile pesticides in greenhouses, residential, and certain outdoor settings, EPA is proposing to expand the requirement from terrestrial food crop to terrestrial feed crop and nonfood, greenhouse food crop and nonfood, forestry, and residential outdoor uses on a conditional basis. This requirement is based on use patterns and other pertinent factors including but not limited to Henry's law constant (the solubility of a gas is directly proportional to the partial pressure exerted by the gas). In combination with volatility studies, this information is needed to develop a profile of the pesticide in the atmosphere. In view of methodological difficulties with the study, including, but not limited to, wall effects, the test note has been amended to recommend consultation with the Agency before tests are performed.

v. *Anaerobic aquatic metabolism.* EPA proposes to require this study (guideline 835.4400) for terrestrial food crop, feed crop, and terrestrial nonfood uses where the pesticide is likely to move from the site of application to nearby aquatic systems. Anaerobic aquatic metabolism studies measure the formation of pesticide residues in water and hydrosoil under anaerobic or oxygen-poor conditions. Since the degradation or dissipation rates and pathways of pesticides in aquatic systems can be different from those of terrestrial systems, soil metabolism studies alone may not be adequate to cover these use patterns.

vi. *Aerobic aquatic metabolism.* The Agency is clarifying that this requirement (guideline 835.4300) applies to aquatic residential uses, and is proposing to expand this requirement to include terrestrial food crop, feed crop, and nonfood, and forestry uses. Aerobic aquatic metabolism studies measure the formation of pesticide residues under aerobic or oxygen-rich conditions in water or sediment while the pesticide is dispersed in aquatic environments. Since the degradation or dissipation rates and pathways of pesticides in aquatic systems can be different from those of terrestrial systems, soil metabolism studies alone may not be adequate to cover these use patterns.

Note also that the Agency is reasserting that Anaerobic Soil Metabolism studies (guideline 835.4200) are required for terrestrial food crop, feed crop, and terrestrial nonfood uses. Due to a printing error, this data requirement was inadvertently omitted from the data tables in 1991 and subsequent publications of the CFR. This action would restore the data requirement in the table. The scope and nature of the requirement would not change.

vii. *Forestry field dissipation.* EPA is proposing to change the status of the forestry dissipation study (guideline 835.6300) from required to conditionally required. Forestry use patterns are broad in scope, range from the application of pesticides to individual trees, to aerial applications covering very large areas, and may apply to tree farms or reforestation efforts. As a result, it is difficult to extrapolate data from tests in particular forestry systems to other forests of regulatory interest. Therefore, this study would need to be tailored to address exposures of concern for particular uses. When the Agency determines that a study is needed, a suggested protocol would need to be submitted and approved by the Agency prior to initiation of the study. The Agency believes that this study will be rarely required. The Agency also proposes to require independent laboratory validation for test methods used to generate data associated with this study to ensure the accuracy and reproducibility of the data, as previously discussed.

viii. *Accumulation in fish.* EPA is proposing minor clarifications to this study requirement (guideline 850.1730). As such, the revised data tables would indicate that this conditional requirement applies to terrestrial feed crop and aquatic residential uses. Further, the Agency proposes to indicate in the test note that studies are required unless:

a. The octanol/water partition coefficients of the pesticide/major degradates are less than 1,000 (indicative of a relatively low potential for accumulation in fish),

b. There are no potential exposures to fish and other nontarget aquatic organisms, or

c. The hydrolytic half-life is less than 5 days at pH 5, 7, and 9.

ix. *Accumulation in aquatic nontarget organisms.* EPA is proposing to expand the conditional requirement for a nontarget aquatic organism accumulation study to terrestrial food crop, feed crop, and nonfood uses; and aquatic food and aquatic nonfood residential uses (guideline 850.1950). The study would be triggered if significant concentrations of the active ingredient and/or its principal degradation products are likely to occur in aquatic environments and may potentially accumulate in aquatic organisms. The Agency proposes to require this study in situations involving direct application of the pesticide to aquatic systems, from various terrestrial sites where run-off or other movement of the pesticide into nearby aquatic systems is likely, or in intercropping situations involving aquatic animal species and traditional aquatic plant crops, *e.g.*, crayfish and rice. The Agency believes that this study will be rarely required.

x. *Confined and field rotational crops.* Because the presence of residues in rotational crops is primarily a dietary risk concern, the Agency proposes to move the data requirements for confined and field rotational crops (guidelines 860.1850 and 860.1900) from environmental fate data requirements to residue chemistry data requirements (subpart O).

xi. *Accumulation studies in irrigated crops.* The Agency proposes to eliminate the environmental fate requirement for the accumulation studies in irrigated crops (formerly guideline 165– 3). Pesticide residue data and information to address the potential for pesticides to be present in crops irrigated with treated water may be obtained from the Magnitude of the Residue in Irrigated Crops study (guideline 860.1540) in subpart O.

XV. Residue Chemistry Data Requirements (Subpart O)

A. General

Residue chemistry data are used by the Agency to estimate people's dietary exposure to pesticide residues from food. The residue chemistry data base is designed to determine the composition of the pesticide residue and how much of that residue is present in the food people eat. Residue chemistry studies include those which define the nature of the residue, *i.e.*, metabolism studies, and those which measure how much of

the residue of concern is present in food, feed, and water, *i.e.*, magnitude of the residue studies. Most food use pesticides require both types of studies. Both plant and livestock metabolism studies are needed to determine the breakdown of the pesticide in a living system, that is, whether the parent compound stays intact or is converted into metabolites. Occasionally, the metabolites are toxic and, as such, are included in the analyses as a residue of concern. Magnitude of the residue studies, also called residue field trials, are done for all foods, such as, fruit and vegetable crops, processed foods, meat and poultry products (including milk and eggs), potable water, fish, and other instances where food may be exposed to pesticide treatment.

In addition to dietary risk assessments, residue chemistry data are used to establish pesticide tolerances which, in turn, are used for enforcement purposes (see Unit XV.B. below). Therefore, methods for detecting the presence and amount of the residue are needed. Detection methods are used by EPA for study validation purposes, and by FDA, USDA, and the states for food inspection purposes.

EPA is proposing changes to the residue chemistry data requirements to better estimate dietary exposure to pesticide residues in or on food or feed, to more accurately assess and reassess tolerances and tolerance exemptions, and to provide additional tools for the enforcement of pesticide residue tolerances to ensure that food entering the commercial market meets the ''reasonable certainty of no harm'' standard under FFDCA. The Agency is proposing to codify data needs that have evolved since the 1984 regulations were issued, and clarify and simplify existing data requirements.

B. Tolerances

1. *Residue chemistry data*. Residue chemistry data are used to assess human dietary exposure and establish tolerances (or tolerance exemptions) for pesticide residues present in food and feed. Pesticide tolerances are listed in 40 CFR part 180. Tolerances are used primarily for enforcement purposes and represent the maximum legal amount of pesticide residue allowed in or on food or animal feed in interstate commerce. Results from data generated from crop field trials are used to set the tolerance for that particular crop. A tolerance or exemption from tolerance must be established for a pesticide to be registered under FIFRA for uses on the food or feed, and for food or feed bearing pesticide residues to be imported into the United States. Wherever possible, EPA tries to harmonize its tolerances with Maximum Residue Levels (MRLs) established by other countries.

2. *Import tolerances*. In cases where a pesticide is not registered in the United States, interested persons may submit a petition requesting that EPA establish a tolerance or tolerance exemption for residues of a pesticide in or on a commodity to allow that treated commodity to be legally imported. These tolerances, called import tolerances, can be established for any food or feed commodity, but are usually established for foods grown outside the United States and its territories, such as bananas or coffee. For new tolerances with no accompanying U.S. registration, part 158 will require that tolerance petitioners provide the information and/or data necessary to make the required safety finding under FFDCA. While there is generally no distinction in data requirements between an import tolerance and any other tolerance issued by EPA, some important differences occur in the way data is generated. This usually includes residue data representative of the pesticide's use in the exporting country. EPA issued proposed guidance for registrants of import tolerances in June 2000 (65 FR 35069). EPA expects to issue its final guidance on import tolerances in the near future.

C. Proposed Residue Chemistry Data Requirements

The residue chemistry data table has been modified to include general use patterns that include food uses, plus the residential outdoor use pattern. EPA is not proposing significant changes to the residue chemistry data requirements from those currently listed in part 158. Two data requirements would be added as separate requirements in the data table. These data (storage stability and multiresidue methods) have been imposed by the Agency on a case-by-case basis. The Reduction In Residue study is now called ''anticipated residues;'' a longstanding independent method validation is being proposed; and two residue studies, confined and field rotational crops, which were formerly environmental fate data requirements, would be moved to the residue chemistry data requirements. Other changes include changes in test substance, conditions under which the test is required, and clarification of test notes. These are not expected to substantively increase the nature or burden of the existing data requirement.

1. *Newly imposed data requirements.* None.

2. *Newly codified data requirements*—i. *Storage stability*. The Agency proposes to add a storage stability study (guideline 860.1380) as an explicit requirement to validate the Magnitude of the Residue studies. Magnitude of the residue studies address how levels of pesticide residues in samples of human foods and livestock feeds are determined. These samples are often stored for extended periods of time prior to analysis. Since tolerances are based on residues at the time of harvest (or sample collection) and the residues may be lost by processes such as degradation and volatilization during storage prior to analysis, storage stability data depicting the presence of residues during this period are critical to validation of the results of the field trial studies. Such data have been required previously as a part of the magnitude of the residue studies, but will now be codified as a separate requirement in the data tables.

ii. *Multiresidue methods.* The Agency also proposes to codify a multiresidue methods study (guideline 860.1360) as a separate requirement. Multiresidue methodology data are currently part of the residue analytical method requirement. These data are important in designing pesticide monitoring and enforcement programs, and as such, multiresidue methodology data is being proposed as a separate requirement. In food monitoring programs, it is not practical or feasible to test for individual pesticides. Since the residue analytical method requirement is intended to refer to a method that is specific for one pesticide (sometimes called a ''single residue method'') and the multiresidue procedures currently used are designed to measure as many pesticides as possible, it is clearer to list these as two separate data requirements. The Agency will amend the test note to stress that any analytical methodology must be evaluated for its ability to detect metabolites included in the tolerance expression.

3. *Revised data requirements*—i. *Nature of the residue in livestock*. Also called an animal metabolism study, EPA is proposing several small changes to the Nature of the Residue in Livestock Study (guideline 860.1300). First, the Agency proposes to require livestock metabolism studies whenever a pesticide is applied to crops used for livestock feed and would indicate this change in the test note for this study. In 1984, livestock metabolism studies were conditionally required and were triggered by the presence of residues in the livestock feed. The Agency changed its policy in July 1989 and now proposes to incorporate it by regulation. The data provides essential information

on the potential transfer and bioconcentration of residues in meat and milk for all pesticides applied to feed items. Therefore, in cases where pesticide misuse results in residues on feed items not expected to have residues from approved uses, the Agency will have data from which to estimate the potential residues in the affected animal commodities.

The Agency is also proposing to change the test substance for this study from the pure active ingredient, radio-labeled (PAIRA) ''and plant metabolites'' to the PAIRA ''or plant metabolite.'' The test substance ''metabolites'' will be changed to ''metabolite'' to prevent dosing with more than one compound in any one study. This is needed because in studies involving simultaneous dosing with both the active ingredient and plant metabolites, it is impossible to determine the amount of metabolite due to active metabolism from that introduced through dosing. Simultaneous dosing with the active ingredient and any metabolites may not produce useful results, because the active ingredient and metabolites may have different metabolic pathways that cannot be differentiated. In most cases dosing with only the parent compound is necessary. However, in cases where plant and animal metabolites are found to differ, a separate study in which livestock are dosed with a unique plant metabolite may also be required.

The livestock metabolism study would be required when a pesticide is applied to livestock premises or is used in livestock drinking water. Such applications may result in both oral and dermal exposure of animals to the pesticide and, depending on the results, may precipitate magnitude of the residue studies to quantify the residues in meat, milk, poultry, and eggs. Finally, the Agency proposes to delete the conditional requirement for the nature of the residue in livestock study for residential outdoor uses since livestock are not found in this use pattern.

ii. *Residue analytical methods.* Residue analytical methods are used to validate the residue field trial studies in plant and animal commodities and as a means of enforcement of established tolerances. The Agency proposes to change the test substance for residue analytical methods (guideline 860.1340) from the ''TGAI and metabolites'' to the ''residue of concern.'' This will focus the study on only those chemicals with potential toxicity, typically the pure active ingredient and other compounds of concern (*i.e.*, metabolites and degradates), and not on the other components of the TGAI.

As part of this data requirement, the Agency is also proposing to require an independent laboratory validation of residue analytical methods to ensure the accuracy and reproducibility of data used for tolerance enforcement purposes. As previously discussed, this policy has been in place since 1988.

iii. *Magnitude of the residue in processed food and feed.* The Agency proposes to change the test substance for processing studies (guideline 860.1520) from an end-use product (EP) to a ''typical'' end-use product (TEP). A processing study is needed for only one representative end-use product proposed for use on a given commodity or site. For a given active ingredient, the Agency believes that, in general, variations of the formulation will not affect the behavior of the active ingredient with respect to processing a raw agricultural commodity bearing residues of that chemical. This change would codify a longstanding practice in EPA.

iv. *Magnitude of the residue in meat, milk, poultry, and eggs.* In line with the livestock metabolism study, the Agency proposes to change the test substance for the meat/milk/poultry/egg study (guideline 860.1480). Due to the difficulties in interpreting results of studies in which a mixture is fed, the Agency is currently discouraging the feeding of mixtures and is instead requesting the feeding of isolated compounds in livestock studies. Hence, the test substance will be changed to read a single plant metabolite instead of metabolites in the plural. Provided that plant and animal metabolites are the same, the parent compound must be the test substance in livestock feeding studies. If any plant metabolite exists that is not also an animal metabolite, a separate feeding study may be required involving dosing with that unique plant metabolite. The Agency will inform the applicant when this additional testing is required. It is rare that this study is requested.

Unlike the livestock metabolism studies, however, livestock feeding studies are generally not required when residues are not demonstrated to be present in the feed. The Agency proposes to clarify that data generally are not required when:

1. Residues are not found on feed items or

2. Livestock metabolism studies indicate minimal transfer of the pesticide residue to tissues, milk or eggs. For those pesticides which leave non-detectable or low residues in feed items and for which the livestock metabolism study shows little transfer of radioactivity to tissues, the Agency may be able to conclude that data on the level of residues in livestock and their byproducts are not necessary.

v. *Magnitude of the residue in potable water, fish, and irrigated crops.* Like the study for processed food and feed commodities, the Agency proposes to change the test substance from an EP to a TEP to determine pesticide residues in potable water, fish, and irrigated crops (guideline 860.1400). Residue data are needed for only one representative end-use product of each formulation type proposed for use on a given commodity or site. For each formulation type for a given active ingredient, the Agency believes that, in general, variations of the formulation will not affect the behavior of the active ingredient.

vi. *Anticipated residues.* The Agency proposes to change the title of the Reduction of Residue study to Anticipated Residues. The new title emphasizes the Agency's intent to use, where appropriate and feasible, data showing the actual residues in food as consumed, as opposed to residues in crops at harvest. For example, market basket surveys can be one way of generating better dietary exposure estimates. The Agency also proposes to indicate in the test note that alternative data, such as market basket surveys, may be required.

The Agency also proposes to add a test note to this study to address the need for residue data on acutely toxic pesticides in single servings of raw agricultural commodities. Most residue data provided to the Agency are based on composited samples. For example, 20 apples collected from different trees may be blended together prior to determining the pesticide residues. This procedure is adequate for estimating dietary risk from pesticides whose toxic effects arise from exposure over a long time period; however, data on composited samples may not be adequate for assessing acute risk from ingestion of single servings of a raw agricultural commodity bearing pesticide residues (*e.g.*, one apple). This proposed analysis of single serving sizes will allow the Agency to more accurately assess acute dietary risks. This additional study would be required only where commodities are consumed in single serving amounts. Historically, the Agency has only asked for this study once. EPA expects that the utility of this study would be for old chemicals with risk concerns. However, for newer chemicals (*e.g.*, reduced risk chemicals) which are the focus of these data requirements, this requirement would rarely be invoked.

vii. *Confined and field rotational crops.* Because the presence of residues

in rotational crops is primarily a dietary risk concern, the Agency proposes to move the data requirements for confined and field rotational crops (guidelines 860.1850 and 860.1900) from an environmental fate requirement (subpart N) to subpart O. The Agency also proposes to revise the test note addressing the requirement for the Field Rotational Crop study. Currently, a Field Rotational Crop study is required when significant pesticide residues are found in the soil at the time of planting. The use of soil residues alone to predict crop residues does not take into account the metabolites of chemicals in the soil and the differing abilities of plants to take up such residues. Since the confined study involves the actual measurement of residues in rotational crops under worst-case conditions, the Agency believes that it is more appropriate to use the results of the Confined Rotational Crop study as a screen for potential residues in crops grown under field conditions and the footnote for the field study will be revised to reflect this approach.

XVI. Applicator Exposure Data Requirements (Subpart U)

A. General

Individuals who handle pesticides are subject to potential risks stemming from pesticide exposure. Because of this, exposure data tailored specifically to address pesticide handlers are crucial. Pesticide handlers (*i.e.*, applicators) are persons who mix, load, apply, or otherwise come into contact with pesticides during the application process. An applicator can be a professional or a homeowner. The risks to applicators is evaluated based upon the results of the toxicity and human exposure studies. Monitoring data are used to quantify the exposure. The proposed data requirements for applicator exposure would allow the Agency to conduct improved exposure assessments for those who handle pesticides.

The current data requirements in part 158 do not contain studies to determine applicator exposure from pesticide use. The Agency, however, has long been aware of the necessity for applicator data to assess the risks from handling pesticides and has frequently asked for such data. In 1987, the Agency published guidelines for such studies. Since that time, applicator exposure studies have been requested when specific exposure and toxicity criteria triggers were met. Since EPA believes these data are essential for fulfilling its mandate to protect human health from pesticide risk, including aggregated and cumulative risks, it is proposing to make the applicator exposure studies a standard part of its regulatory data requirements.

EPA proposes to codify requirements for application exposure data in part 158 as a new subpart U. The purpose of codifying these data requirements is to assist pesticide registrants and others in determining which studies are required, and aid them in designing and conducting field studies that measure potential dermal and respiratory exposure to pesticides during handling activities. These test requirements cover exposure monitoring studies for people involved in mixing, loading, and applying pesticides; flagging during aerial applications; and other tasks, such as cleaning of equipment and spill cleanup that result in direct contact with pesticides. The requirements cover not only agricultural applicators, but other occupational applicators and residential applicators as well.

B. Criteria for Testing

The Agency proposes to establish toxicity and exposure criteria for applicator exposure studies. These criteria are based on the toxicity of the active ingredient and the proposed exposure pattern of the product.

1. *Toxicity criteria.* EPA proposes that applicator exposure data be required for occupational and residential exposures for pesticide active ingredients that indicate potential adverse effects from toxicity studies, such as developmental toxicity, carcinogenicity, neurotoxicity, reproductive toxicity, immunotoxicity, 90–day oral toxicity, 21–day dermal toxicity, 90–day inhalation toxicity, and chronic feeding.

Specifically, EPA is proposing that the toxicity criteria be based on the toxicity of the active ingredient. Applicator exposure monitoring data would be required, as determined by the Agency, if the active ingredient meets any of the following criteria:

i. Evidence of potentially significant adverse effects have been observed in applicable toxicity studies. For example, toxicity studies may indicate that the active ingredient is a possible or likely human carcinogen and that carcinogenic risk can be assessed using a linear extrapolation approach with a Q_1*. Or, toxicity studies may indicate that the active ingredient may cause developmental, neurotoxic, reproductive, or immunotoxic effects or may inhibit cholinesterase and establish a toxicological endpoint of concern that can be used to assess risks to applicators and other handlers.

ii. Scientifically sound epidemiological or poisoning incident data indicate that adverse health effects may have resulted from handling of the pesticide. For example, EPA reviews data in the:

a. Office of Pesticide Programs Incident Data System reports of incidents from various sources, including registrants, other federal and state health and environmental agencies and individual consumers);

b. Toxic Exposure Surveillance System (a national data collection system of Poison Control Center data);

c. National Pesticide Information Center database (NPIC is a toll-free information service supported by the Office of Pesticide Programs that fields calls about human and animal incidents); and

d. California Department of Pesticide Regulation exposure incident database. California physicians are required, by statute, to report to their local health officer all occurrences of illness suspected of being related to exposure to pesticides. The majority of the incidents involve workers. CDPR has collected uniform data on suspected pesticide poisonings since 1982.

2. *Exposure criteria.* EPA proposes to establish exposure criteria that would trigger applicator exposure studies. In determining what studies are required, EPA considers the product's use patterns, use surveys, application methods, whether the product is for indoor or outdoor use, whether the exposure is expected to be occupational or residential, the duration of the exposure (*i.e.*, short-term, intermediate-term, or long-term), whether sensitive subpopulations might be exposed, and other criteria. Applicator exposure monitoring studies would be required if either dermal or respiratory exposure is likely to occur during the prescribed use. Applicants are strongly encouraged to consult with the Agency to determine applicable data needs.

Specifically, EPA is proposing the following exposure criteria. Data would be required, as determined by the Agency, if either of the following conditions is met:

i. Dermal exposure is likely to occur when used as directed on the label,

ii. Respiratory exposure is likely to occur when used as directed on the label.

Because these exposure scenarios are covered under the broad categories of occupational and residential, the table in § 158.1520 lists only these two use patterns.

The Agency may also require data when exposure is likely, when the pesticide is used in a commonly recognized and widespread manner. Thus, if the Agency knows that a

particular product or class of products is frequently used in a manner that isn't directed on the label, the Agency can still require data.

C. Proposed Applicator Exposure Data Requirements

1. *Newly imposed data requirements.* None.

2. *Newly codified data requirements.* EPA is proposing seven separate data elements for applicator exposure data.

i. *Dermal exposure studies.* The Agency proposes to add data requirements for both outdoor and indoor dermal exposure studies (guidelines 875.1100 and 875.1200) in order to estimate the dermal exposure to persons directly handling pesticides. Dermal exposures can and do occur at levels that can cause adverse effects. Dermal applicator exposure studies employ passive dosimetry techniques which estimate the amount of a chemical impinging on the surface of the skin. The amount of pesticide potentially available for absorption through the skin can be estimated by trapping the material before it contacts the skin or by removing the material that has contacted the skin before it has been absorbed.

ii *Inhalation exposure studies.* To estimate occupational and residential human post-application inhalation exposure to pesticide residues, the Agency proposes to add data requirements for both outdoor and indoor inhalation exposure studies (guidelines 875.1300 and 875.1400). Inhalation exposures can and do occur at levels that can cause adverse effects. Protocols must be submitted for approval prior to initiation of the study. Details for developing protocols are available from the Agency.

iii. *Biological monitoring.* Data from biological monitoring studies (guideline 875.1500) provide the Agency with estimates of the internal dose or amount of a pesticide in the body. EPA proposes to allow the submission of biological monitoring data in addition to, or in lieu of, dermal or inhalation exposure data provided the human pharmacokinetics of the pesticide residue is sufficiently understood to permit the back calculation to determine the total internal dose. Biological monitoring offers the advantage of assessing the internal dose, as opposed to the exposure or amount of chemical coming in contact with the surface of the skin or available for inhalation in the lungs as measured using passive dosimetry techniques. Biological monitoring is being proposed as a conditional requirement.

iv. *Data reporting and calculations information.* EPA proposes to require registrants to submit data reporting and calculation information (guideline 875.1600) whenever handler exposure data are submitted. Data reporting and calculations information is important because it allows EPA to assess the quality of an applicator exposure study and the accuracy of the exposure calculations derived from the study. Information that must be submitted includes a description of the purpose of the study and what requirement(s) it is intended to satisfy, a summary of the study, a comprehensive section on materials, methods, and calculations, a section interpreting the scientific results of the study, a discussion of quality assurance, identification of the location of the raw data, and any references, communications, and protocols relevant to the conduct of the study.

v. *Product use information.* EPA is proposing to require product use information (guideline 875.1700) for both the occupational and residential use patterns. Product use information assists EPA to more accurately assess pesticide exposure to applicators by describing how the pesticide is actually used and applied in occupational and residential settings. EPA requires this information because differences in use can translate to significant differences in exposure, and thus risk. The required information is to encompass a description of the application of the pesticide and include the range and typical values for: Application rates; amount of formulated product or active ingredient handled per day and per year or season; acreage or area treated per day and per year or season; timing of and number of treatments per year or season for private and commercial handlers; exposure time per activity; types of handling equipment used, geographical distribution of usage; any available surveys that provide use information, and other relevant use data.

3. *Use of surrogate data.* To support the registration of a pesticide product, EPA encourages applicants and registrants to generate needed exposure data with the particular pesticide product. However, the Agency recognizes the need to impose exposure data requirements judiciously to minimize the economic burdens on applicants, and at the same time, obtain sufficient data and information for exposure and risk assessments. Therefore, whenever possible, surrogate data will be used to assess the occupational and residential exposure to pesticides. Because the Agency does not commonly require these studies and because surrogate data is often available, the Agency does not expect that ''full'' studies will often be needed. However, when surrogate data prove inadequate for the Agency to estimate likely exposures, applicants and registrants would be required to submit the additional data proposed in subpart U.

Surrogate applicator exposure data may adequately satisfy these data requirements under certain circumstances. Surrogate applicator data must be generated using comparable methods and under similar usage conditions as the product under review. Surrogate exposure data estimations must have adequate information to address handler exposure data requirements and must contain adequate replicates of acceptable quality data to reflect the specific use prescribed by the label, including formulation type, application equipment, methods and rates, personal protective equipment, engineering controls and other pertinent use directions or restrictions.

Surrogate data may be obtained from several reliable sources. For many years, the Agency has been expanding its Pesticide Handlers Exposure Database (PHED) which provides surrogate data for a wide variety of handler exposure scenarios. PHED is a generic database containing measured exposure data for persons involved in the handling or application of pesticides in the field and contains data for over 2000 monitored exposure events. Users can select data from each major PHED file (*e.g.*, mixer/loader, applicator, flagger, or mixer/loader/applicator) and construct exposure scenarios that are representative of the use of the chemical. Although the PHED database was originally developed for the agricultural workplace, it now contains information that is applicable to other pesticide use scenarios, including residential settings. In general, PHED is not appropriate for assessing highly volatile or gaseous pesticides (*e.g.*, fumigants). EPA, Health Canada, pesticide registrants, and other interested entities are participating in a task force to update, refine, and expand the handler exposure database.

Some surrogate data for outdoor pesticide applications in residential settings (occupational and residential handlers) also is available through the Outdoor Residential Exposure Task Force. The Task Force has submitted data to the Agency on mixer, loader, and applicator exposures during use of several types of equipment typically found in residential settings. The Agency may accept surrogate exposure data estimations from NIOSH, OSHA,

and OECD to satisfy handler exposure data requirements, if the data meet the basic quality assurance, quality control, good laboratory practice, and other scientific requirements set by EPA. Moreover, if EPA determines that industrial standards, such as the workplace standards set by OSHA, provide adequate protection under the standard set by FIFRA for a particular pesticide use pattern, applicator exposure data may not be required for that use pattern.

XVII. Data Requirements Not Affected by this Proposal

EPA is proposing today a major restructuring of current part 158 for clarity and comprehensibility, but is not proposing substantive revisions to all portions of current part 158. Several specific sections of part 158 may be revised in the future, including the following:

- Section 158.440 Spray drift data requirements
- Section 158.640 Product performance data requirements
- Section 158.690 Biochemical pesticide data requirements
- Section 158.740 Microbial pesticide data requirements

In addition, the Agency intends later to propose other changes to current part 158, including the creation of separate subparts to address data requirements for the registration of antimicrobial pesticide products and biochemical and microbial pesticide products.

In order to accommodate the restructuring of part 158 without creating confusion for readers of this proposal, EPA proposes to revise the Table of Contents for part 158 to include the future subpart designations for these sections, and to add and reserve the appropriate subparts in the revised part 158. The regulatory text of the sections for which no change is proposed is not reprinted in this proposal, and EPA is not requesting comment on any aspect of those unchanged data requirements.

If EPA does not issue these other proposals before this proposal is issued in final form, EPA will transfer the contents of the current part 158 that are not specifically addressed in this proposal into their new subparts, essentially unchanged. This step will be necessary because at that time subpart D which currently contains the sections will be redesignated to contain only product chemistry data requirements.

At the same time, EPA expects to make needed technical revisions to accommodate the new structure of part 158, without changing the substance of the data requirements. For example, section numbers will be assigned within the new subpart; cross-references will be updated; and footnotes will be restructured as test notes and given Arabic numerals, *e.g.*, footnote (iv) would become test note (4). EPA believes these minor technical revisions can be accommodated within the final rule without specific proposal at this time.

XVIII. Peer Review

A. National Research Council Recommendations

In 1988, Congress directed the National Academy of Sciences to study the vulnerability of infants and children to dietary pesticides. The National Research Council was charged with ''examining scientific and policy issues faced by government agencies, particularly EPA, in regulating pesticide residues in foods consumed by infants and children.'' In so doing, the NRC was asked to:

- Examine the adequacy of current risk assessment policies and methods;
- Assess information on the dietary intakes of infants and children;
- Evaluate data on pesticide residues in the food supply;
- Identify toxicological issues; and
- Develop relevant research priorities.

The Council reviewed current EPA practices and data requirements related to dietary risk assessment as well as testing modifications planned by the Agency. In 1993, the NRC issued a report (Ref. 1) entitled, ''Pesticides in the Diets of Infants and Children.'' The panel of experts concluded that, at that time, EPA approaches to data requirements and risk assessments emphasized the evaluation of the effects of pesticides in mature animals and, in general, there was a lack of data on pesticide toxicity in developing organisms.

The Council was not specifically charged with evaluating the data requirements as proposed today. Nonetheless, the Council made recommendations with respect to regulatory needs for data development that EPA is today proposing:

- The report stated the need to investigate the effects of pesticide exposure on immunotoxic responses in infants and children. ''Analysis of the impact or toxicity of agricultural chemicals on the immune system is essential. Regulatory development of a battery of consensus tests is critical to protect the developing immune system.'' (Ref. 1, p. 110).
- The report supported the Agency's proposed requirement for acute and subchronic neurotoxicity testing for pesticides and ''encourages the agency to make this a general requirement for all food-use pesticides.'' (Ref. 1, p. 156).
- The report strongly encouraged further work in the area of developmental neurotoxicity. ''Neurodevelopmental effects must be part of the battery of end points evaluated for toxicants.... Regulatory development of a battery of consensus tests will be .... necessary to ensure public confidence.'' (Ref. 1, p. 110).
- The report suggested that the Agency impose a requirement for developmental toxicity for all classes of pesticides registered for food uses. ''A modified reproductive/developmental toxicity study in the rat is suggested for registration of all food-use pesticides.... the committee recommends that this study be made a requirement for registration for all food-use pesticides.'' (Ref. 1, p. 155)

Other recommendations by the Council included an *in utero* chronic toxicity/carcinogenicity test and the inclusion of thyroid function into existing tests. The Council also recommended a conditional requirement for visual system toxicity testing, especially for cholinesterase-inhibiting compounds. These recommendations were brought to the SAP and are discussed in Unit XVIII.B. Other recommendations arising from the NRC report are still being considered for use on a case-by-case basis, as summarized in the list of potential data requirements in Unit XI.D.

B. FIFRA Science Advisory Panel

In 1994, EPA held a 2-day meeting of the SAP to review the Agency's proposed amendments to the data requirements for pesticide registrations contained in 40 CFR part 158. The SAP was asked to comment on each data requirement and identify, in their opinion, which ones were necessary to fully and thoroughly evaluate the potential hazard of a chemical compound and which ones were not intrinsically useful in providing practical scientific information. The revisions presented to the Panel, *i.e.*, the changes to the data requirements presented in this notice, were generally endorsed. Data requirements, as they related to the application of the newly mandated FFDCA safety factor, were also presented to the SAP in 1998 and 1999. No new issues of a scientific nature have surfaced since these meetings that would warrant SAP review. Copies of documents prepared for the SAP and the final reports from each of the meetings can be found on EPA's web site at *http://www.epa.gov/scipoly/sap*. A copy of the 1994 final report also can be found in the public

docket for this rulemaking. The Panel's comments and conclusions are summarized below.

1. *Terrestrial and aquatic nontarget organisms.* In 1994, EPA requested comment from the SAP on the merits of requiring sediment and pore water toxicity testing to its data requirements for pesticides and whether the Agency's proposed tiered approach is appropriate. The Agency also requested comment on proposals to add additional testing requirements. The Panel believed that the addition of sediment and pore water testing would provide additional useful information and the proposed tiered approach appeared to provide a reasonable sequence of tests. Further, the Panel supported the requirement of both fish early lifestage and invertebrate life-cycle tests for certain aquatic and terrestrial uses and the addition of granular and other typical end-use products in avian oral testing. The SAP agreed that the avian reproduction test be expanded to include all outdoor uses, but the test protocol should be flexible in order to reflect more accurately the environmental fate of the chemical.

2. *Toxicology.* At the 1994 meeting, EPA put forth the revisions to part 158 that included acute and subchronic neurotoxicity studies, as well as immunotoxicity studies in adults as first tier tests. The Agency also included in its presentation several studies recommend by the NRC in their 1993 report. In its final report the SAP offered comments and cited some specific recommendations for improvement.

For the few studies the SAP did not endorse, the Panel could not find a significant scientific justification for the routine use of the data. For example, due to increased concerns about the potential effects of pesticides on the visual system, special visual system testing was suggested by the NRC as a data requirement. The Panel, however, concluded that there was insufficient scientific evidence to require special visual system testing. After reviewing its toxicology data base, at that time, for visual effects, *i.e.*, pathological damage to the eye, EPA found that only five organophosphates and one carbamate exhibited visual effects. Cholinesterase-inhibition was considered the more sensitive endpoint and using this as an endpoint would be protective of the supposed visual system effects. Therefore, since the Agency already was regulating these pesticides at much lower doses than those expected to produce adverse effects on visual systems, it concluded that there was already adequate protection from any possible visual effects.

Similarly, the SAP did not recommend additional testing on *in utero* exposure in carcinogenicity studies, a 90–day drinking water study, nor testing for thyroid function or other endocrine effects in routine chronic studies. Regarding the need to examine the potential perinatal or postnatal toxicity from pesticide residues in the diets of children, the Panel did not believe a special new study was warranted. In each of these instances the SAP thought it was premature to include a data requirement in part 158 until methods have been scientifically validated and guidelines developed, and the data could be scientifically evaluated to yield meaningful results.

In 1998, EPA presented the SAP an issues paper on the use of the FQPA safety factor to address the special sensitivity of infants and children to pesticides. Here the Agency presented the Panel another, and more detailed, discussion of the toxicology data base, especially in regard to developmental neurotoxicity testing criteria and requirements. The developmental neurotoxicity study specifically was put in the context of the appropriateness of a possible additional safety factor. At that time, the SAP did not reach a consensus on whether this study should be routinely or conditionally required. The issue of what is a complete and reliable data set was brought before the SAP again in May 1999. The majority of the Panel supported the Agency's approach to applying data requirements but advised the Agency to revisit the first tier toxicology data base every few years to update data requirements as needed. The Panel also agreed with the Agency in the need to require the neurotoxicity battery of studies, including developmental neurotoxicity testing, for new conventional high exposure, *i.e.*, food use, pesticide registrations.

3. *Nontarget plant protection.* In 1994, EPA presented the SAP with its plant protection data requirements. The SAP was asked to provide specific information or guidance on a number of issues. The SAP supported the elimination of the seed germination test. In addition, the Panel recommended changing the test substance from the technical grade active ingredient to the typical end-use product for terrestrial plant studies and eliminating Tier I testing of phytotoxins on terrestrial plants.

4. *Occupational and residential exposure.* Data requirements for exposure assessment for both applicators and those exposed to pesticides post-application were presented to the SAP in 1994. The Agency did not present any specific questions on exposure assessment for application or post-application exposure, and, by comparison to other subparts addressed in the response, the SAP had relatively few comments on data revisions for exposure monitoring and assessment. Several areas of clarification were advised, especially with regard to what data would be needed for what use patterns. It was also suggested that the Agency work with representatives from industry to develop a clear set of guidelines for both residential and occupational settings.

Working in collaboration with Health Canada, and OECD, EPA drafted guidelines for post-application exposures studies. They were peer-reviewed by EPA's Office of Research and Development, the California Department of Pesticide Regulation, representatives from academia, and the American Crop Protection Association. The Agency presented its post-application exposure guidelines and standard operating procedures to the SAP in 1998 and again in 1999. In 1999, the SAP approved and commended the Agency for making significant strides toward developing scenario-based residential and non-occupational exposure assessments that are sufficiently conservative as to not underestimate exposures. (Ref. 11)

5. *Environmental fate.* Three of the significant changes that the Agency is proposing for the environmental fate data requirements, *i.e.*, conditionally requiring aerobic soil metabolism and terrestrial field dissipation for aquatic uses involving sites that are intermittently dry, and conditionally requiring ground water monitoring for terrestrial and forestry use, were presented to the SAP at the 1994 meeting. The SAP endorsed these changes as well as the independent laboratory validation of analytical methods.

6. *Residue chemistry.* In 1994, EPA presented the SAP with its residue chemistry data requirements. While no specific questions were directly posed to the Panel, the SAP made a few comments. The SAP endorsed the independent laboratory validation of analytical methods, the establishment of a separate data requirement for multiresidue methodology, and a requirement for storage stability data. In addition, the Panel supported the Agency's efforts to identify the circumstances under which single serving analyses would be needed for acutely toxic pesticides.

XIX. International Harmonization of Data Requirements

EPA is working closely with other countries toward greater uniformity in testing, reviewing and evaluating pesticides. The benefits of international regulatory cooperation on pesticides are potentially great: improved science through greater information exchange, and reduced regulatory and resource burdens on national governments and regulated parties through harmonized pesticide registration review. Over the last several years, substantial progress has been made toward international cooperation on pesticide regulatory review. Member countries of the OECD, including the United States, have agreed upon harmonized guidance for the formats of industry data submissions (dossiers) and country data review reports (monographs). Countries now frequently exchange pesticide reviews or consult with one another on key technical aspects of a review. EPA has worked jointly with Canada, dividing up detailed evaluation work on a number of pesticides. The Agency has entered into information exchange and comparative review arrangements on a pilot basis with other countries, as well. The objective of these work sharing arrangements has been to pool scientific knowledge and to use resources in the most efficient way possible.

As the international regulatory community works toward greater harmonization on pesticide review, attention has turned to data requirements, how they compare from one country to another and what can or should be done to establish common requirements. To the extent that data requirements for pesticide registration are similar, sharing reviews and comparing evaluations is easier and more meaningful. Establishing similar requirements also can reduce the resources that must be spent to conduct testing. Requirements that differ considerably from one country to another can mean that registrants who are looking to register a pesticide in more than one country must conduct many different studies to satisfy all the various national requirements.

The United States and Canada have worked together to harmonize data requirements across all disciplines. Data requirements and protocols for the two countries have been carefully compared. The data requirements proposed in this document represent U.S. national requirements but they reflect extensive consultation with Canada and are harmonized with Canada's requirements to a high degree. The two countries plan to continue to work together to keep data requirements for all disciplines as similar as possible.

OECD Member countries have had discussions about harmonizing data requirements within the OECD community. The pesticide industry took on the complex task of looking at data requirement differences among Member countries to identify areas that might benefit from harmonization. They presented their preliminary findings to the OECD Working Group on Pesticides meeting in June 2001. They reported, consistent with the positions of scientific reviewers in OECD Member countries, that toxicology data requirements are quite similar across countries. Issues can arise sometimes, however, because study protocols or guidelines used to generate the studies to meet the requirements are not always harmonized. In other words, a particular study requirement might be the same from one country to the next, but the study submitted to meet the requirement can run into problems if done according to a protocol that is acceptable in one country but not another. Overall, however, it appears that reasonable harmonization has been achieved for toxicology studies done according to OECD Guidelines revised since 1997. This does not mean that there is no room for additional harmonization work on toxicology data requirements and study guidelines, but rather that there are other testing areas where there is much less consistency on data requirements and study protocols across countries.

Ecotoxicological and environmental fate studies present a particular challenge for harmonization. Data requirements in these areas can differ considerably from one country to another depending upon how countries' tiered approaches to data requirements are applied. National data requirements have to be tied to national use patterns and environmental and ecological conditions. A reliable environmental hazard assessment, for example, must be based on studies that accurately reflect the climate, soil types and agricultural practices of the country doing the assessment. Because ecological and environmental studies must be representative of national conditions to adequately support national risk assessments, harmonization of data requirements and study protocols for these types of studies can be difficult. Harmonization can require extensive dialogue between scientists to determine which data requirements can act as common requirements. Harmonization can also involve protocol/guideline development or revisions in order for the studies produced to meet common data requirements to be widely accepted.

XX. Research Involving Human Subjects

In the United States, all research with human subjects conducted or supported by the Federal government is governed by a set of regulations referred to as the Common Rule. The Common Rule contains requirements designed to protect human subjects of research and to ensure that they are treated ethically. EPA, along with 16 other federal departments and agencies, promulgated the Common Rule in 1991. See 40 CFR part 26 (EPA's Common Rule). In all of the scientific research with human subjects conducted or supported by EPA, the Agency has been and remains committed to full compliance with the Common Rule

Both the current version of part 158 and the version of part 158 being proposed contain requirements for the conduct of studies that involve testing with human participants. These studies include: metabolism and pharmacokinetic studies, biological monitoring studies, human exposure studies, and insect repellent efficacy studies. It should be noted that neither the current nor proposed version of the part 158 contains a provision that requires testing of human participants in a study designed to identify or quantify a toxic endpoint. If studies required under part 158 were conducted or supported by EPA (or another Federal agency), they would be subject to the Common Rule. Although the Common Rule applies only to research conducted or supported by Federal agencies, EPA recognizes that many public and private research and academic institutions and private companies, both in the United States and in other countries, including non-federal U.S. and non-U.S. governmental organizations, have their own specific policies related to the protection of human participants in research.

EPA has been considering its policies and rules regarding the conduct of studies involving human participants by organizations that are not part of the Federal government and that do not receive support from a Federal agency. (These are referred to as ''third party'' researchers). On February 8, 2005 (70 FR 6661)(FRL–7695–4), EPA issued a **Federal Register** Notice announcing that it plans to conduct rulemaking to make the provisions of the Common Rule, 40 CFR part 26, applicable to certain newly conducted third-party human studies. The Notice also indicated that EPA may propose to adopt some or all of the Department of Health and Human

Services' (DHHS) protections for research with vulnerable populations. The DHHS rules are contained in 45 CFR part 46, subparts B (pregnant women, human fetuses, and neonates), C (prisoners), and D (children) and apply when members of these groups are being considered as potential participants in covered research.

XXI. ILSI Work on New Toxicity Paradigm

The Health and Environmental Sciences Institute (HESI)/International Life Sciences Institute initiated a project in 2001 titled ''Developing Strategies for Agricultural Safety Evaluation.'' The purpose of this project was to bring together scientific experts from government, academia and industry, including the international community to determine whether the current testing paradigm for pesticide chemicals could be made more efficient and accurate. Agency scientists from EPA's Office of Pesticide Programs and Office of Research and Development are involved in this project. The HESI technical work groups have developed a tiered approach that takes into account the toxicological properties and the use pattern of the chemicals, and attempts to minimize the number of animals necessary to produce a thorough health assessment of the chemicals of interest. The HESI reports are anticipated to be submitted for publication in the *Journal Critical Reviews and Toxicology*, April 2005. The draft HESI papers can currently be viewed in PDF format at *http://hesi.ilsi.org/publications/pubslist.cfm?publicationid=578*. Once the reports are published (anticipated for summer 2005), the Agency will consider the HESI tier approach, as well as other available proposals on toxicology testing including the ongoing National Academy of Sciences project on the future of toxicology testing, to determine what revisions to current testing guidelines and data requirements may be appropriate. Before considering regulatory approaches, the Agency will need to develop scientific position papers concerning the new approach for Agency internal and external review (including review by the FIFRA Science Advisory Panel), and public comment. Regulatory changes will be made, as needed, to keep the data requirements current, as stated in proposed § 158.30(b).

Information on the HESI project can be found at the following website: *http://hesi.ilsi.org/index.cfm?pubentityid=55.* Information on the NAS project can be found at the following website: *http://www4.nas.edu/webcr.nsf/5c50571a75df494485256a95007 a091e/f6b42dd0563b352e85256e5d0007281e.*

XXII. Animal Welfare Concerns

The Agency is committed to the development and use of alternative approaches to animal testing. The Agency understands many people's concern about the use of animals for research and data development purposes. EPA has received comments concerning the use of new and revised test methods which would reduce the number of test animals in studies, or refine procedures to make them less stressful to animals. Where testing is needed to develop scientifically adequate data, the Agency is committed to reducing or replacing, wherever possible, the number of animals used for testing by incorporating *in vitro* (non-animal) test methods or other alternative approaches that have been scientifically validated and have received regulatory acceptance. EPA considers these goals and commitments to be important considerations in developing health effects data, consistent with the essential need to conduct scientifically sound chemical hazard/risk assessments in support of the Agency's mission.

Taking into consideration principles of sound science and the requirements of FIFRA to protect humans (including sensitive subpopulations) and the environment from unreasonable uncertainty of no harm from pesticide exposure, the Agency is committed to avoiding unnecessary or duplicative animal testing. For example, currently EPA accepts data on the pH of a chemical as a screen to judge whether the chemical may be corrosive to the eye or skin. Making this determination avoids actual testing on animals. Many long-term studies can be combined so that several toxicological end-points can be discerned from fewer studies. The Agency already has bridging and batching policies in place to allow the use of acute toxicity, sensitization, or irritation test data on products to be used to support other products. At EPA's initiative, these policies have been incorporated into the new Globally Harmonized System for Classification and Labeling.

The Agency plays an important role in the Federal Interagency Committee for the Validation of Alternative Methods (ICCVAM) (*http://iccvam.niehs.nih.gov/home.htm*). ICCVAM, a standing committee made up of 15 federal agencies and established through the National Institute of Environmental Health Sciences, which works to:

1. Encourage the reduction of the number of animals used in testing.

2. Seek opportunities to replace test methods requiring animals with alternative test methods when acceptable alternative methods are available.

3. Refine existing test methods to optimize animal use when there is no substitute for animal testing.

ICCVAM convenes independent peer review panels to evaluate specific proposed test methods and has developed consensus criteria for judging the validation status of test methods.

Guideline 870.1100 references the use of appropriate alternative test protocols as a means of reducing the number of animals used to evaluate acute effects of chemical exposure. Yet the Agency and the scientific community also recognize that test guidelines are designed to be updated and supplemented frequently. As new tests and test batteries are validated, the Agency presents them to the SAP. The Agency considers the SAP's determination of the reliability of the test guidelines and their applicability to meeting its regulatory needs under FIFRA. After SAP review, the Agency is planning to incorporate validated *in vitro* screening data for skin corrosion to its test guidelines. As other appropriate alternative or *in vitro* methods become available, they will continue to be added to the test guidelines.

XXIII. Summary of Changes Being Proposed

Table 3 contains a line-by-line listing of every data requirement contained in current part 158, as well as new requirements proposed today, organized in the order of the proposed new subparts D through U. Columns 1 and 2 contain Pesticide Assessment Guideline numbers and current titles, respectively. Columns 3 and 4 contain OPPTS Harmonized Guidelines numbers and proposed titles, respectively. Column 5 contains an explanation of the changes proposed for each requirement, or that no change is proposed.

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
Subpart D—Product Chemistry and Guideline No.				
Product Identity and Composition				
61–1	Product composition	830.1550	Product identity and composition	No changes.
61–2	Description of materials used to produce the product	830.1600	Description of materials used to produce the product	No changes.
61–2	Description of production process	830.1620	Description of production process	No changes.
61–2	Description of formulation process	830.1650	Description of formulation process	No changes.
61–2	Discussion of formulation of impurities	830.1670	Discussion of formulation of impurities	No changes.
62–1	Preliminary analysis	830.1700	Preliminary analysis	No changes.
62–2	Certified limits	830.1750	Certified limits	No changes.
62–3	Enforcement analytical method	830.1800	Enforcement analytical method	No changes.
64–1	Submittal of samples	830.1900	Submittal of samples	No changes.
Physical and Chemical Properties				
63–2	Color	830.6302	Color	No changes.
63–3	Physical state	830.6303	Physical state	No changes.
63–4	Odor	830.6304	Odor	No changes.
63–5	Melting point	830.7200	Melting point/melting range	No changes.
63–6	Boiling point	830.7220	Boiling point/boiling range	No changes.
63–7	Density, bulk density, or specific gravity	830.7300	Density/relative density/bulk density	Clarified test note to better identify when this test requirement is applicable.
63–8	Solubility	830.7840 830.7860	Water solubility	No changes.
63–9	Vapor pressure	830.7950	Vapor pressure	Clarified test note to better identify when this test requirement is applicable.
63–10	Dissociation constant	830.7370	Dissociation constants in water	Clarified test note to better identify when this test requirement is applicable.
63–11	Octanol/water partition coefficient	830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)	Changed from ''conditionally required'' to ''required.''
63–12	pH	830.7000	pH	No changes.
63–13	Stability	830.6313	Stability to normal and elevated temperatures, metals, and metal ions	Changed from ''required'' to ''conditionally required.''
63–14	Oxidizing or reducing action	830.6314	Oxidation/reduction: chemical incompatability	No changes.
63–15	Flammability	830.6315	Flammability	No changes.
63–16	Explodability	830.6316	Explodability	Changed from ''required'' to ''conditionally required.''

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
63–17	Storage stability	830.6317	Storage stability	No changes.
63–18	Viscosity	830.7100	Viscosity	No changes.
63–19	Miscibility	830.6319	Miscibility	No changes.
63–20	Corrosion characteristics	830.6320	Corrosion characteristics	No changes.
63–21	Dielectric breakdown voltage	830.6321	Dielectric breakdown voltage	No changes.
	None	830.7050	UV/visible light absorption	Proposed requirement.
	None	830.7520	Particle size, fiber length, and diameter distribution	Proposed conditional requirement.
Subpart E—Nontarget Organisms Data Requirements				
Avian and Mammalian Testing				
71–1	Avian oral LD_{50}	850.2100	Avian oral toxicity	Added testing on a second species (passerine) for some uses. Expanded requirement to include testing with the TEP. Clarified test note to better identify when this test requirement is applicable.
71–2	Avian dietary LC_{50}	850.2200	Avian dietary toxicity	Changed from ''conditionally required'' to ''not required'' for greenhouse and indoor uses. Added a conditional requirement for testing one avian species for aquatic nonfood residential uses. Data on a second avian species may also be required.
71–3	Wild mammal toxicity	850.2400	Wild mammal toxicity	Clarified test note to better identify when this test is applicable.
71–4	Avian reproduction	850.2300	Avian reproduction	Changed from ''conditionally required'' to ''required'' for terrestrial, aquatic food, aquatic nonfood outdoor, forestry, and residential outdoor uses.
71–5	Simulated or actual field testing-mammals and birds	850.2500	Simulated or actual field testing	Expanded conditional requirement to terrestrial feed and aquatic nonfood outdoor uses. Added independent laboratory validation of methods.
Sediment Testing				
	None	850.1735 850.1740	Whole sediment—acute invertebrates (freshwater and marine)	Proposed conditional requirement.
	None	None	Whole sediment—chronic invertebrates (freshwater and marine)	Proposed conditional requirement.
Nontarget Insect Testing				
141–1	Honey bee acute contact LD_{50}	850.3020	Honey bee acute contact toxicity	Changed from ''conditionally required'' to ''required'' for all terrestrial, aquatic food, aquatic nonfood outdoor, forestry, and residential outdoor uses.
141–2	Honey bee—toxicity of residues on foliage	850.3030	Honey bee—toxicity of residues on foliage	Clarified test note.
141–4	Honey bee subacute feeding study	141–4	Honey bee subacute feeding study	Eliminated requirement.

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
141–5	Field testing for pollinators	850.3040	Field testing for pollinators	Expanded conditional requirement to terrestrial feed and aquatic nonfood (outdoor and residential) uses.
142–1	Acute toxicity to aquatic insect	142–1	Acute toxicity to aquatic insect	No changes.
142–1	Aquatic insect life-cycle study	142–1	Aquatic insect life-cycle study	No changes.
142–3	Simulated or actual field testing for aquatic insects	142–3	Simulated or actual field testing for aquatic insects	No changes.
143–1 143–2 143–3	Nontarget insect testing—predators and parasites	143–1 143–2 143–3	Nontarget insect testing—predators and parasites	No changes.
Aquatic Organism Testing				
72–1	Freshwater fish LC_{50}	850.1075	Freshwater fish toxicity	Added conditional requirement for a second species of fish for greenhouse and indoor uses. Added testing requirement using the TEP.
72–2	Acute LC_{50} freshwater invertebrates	850.1010	Acute toxicity freshwater invertebrates	No changes
72–3	Acute LC_{50} estuarine and marine organisms	850.1025 850.1035 850.1045 850.1055 850.1075	Acute toxicity estuarine and marine organisms	Changed from ''conditionally required'' to ''required'' for terrestrial, aquatic (food and nonfood outdoor), residential outdoor, and forestry uses; changed the aquatic nonfood residential use to ''not required.''
72–4	Fish early-life stage and Aquatic invertebrate life-cycle	850.1300	Aquatic invertebrate life-cycle (freshwater)	Changed from ''conditionally required'' to ''required'' for terrestrial, aquatic (food and nonfood outdoor), and forestry uses. Changed the aquatic nonfood residential use to ''not required.''
72–4	None	850.1350	Aquatic invertebrate life-cycle (saltwater)	Expanded the conditional requirement to include terrestrial feed and aquatic nonfood outdoor uses. Changed the aquatic nonfood residential use to ''not required.''
72–4	None	850.1400	Fish early-life stage (freshwater)	Changed from ''conditionally required'' to ''required'' for terrestrial, aquatic (food and nonfood outdoor), and forestry uses. Changed the aquatic nonfood residential use to ''not required.''
72–4	None	850.1400	Fish early-life stage (saltwater)	Expanded the conditional requirement to include terrestrial feed and aquatic nonfood outdoor uses. Changed the aquatic nonfood residential use to ''not required.''
72–5	Fish life-cycle	850.1500	Fish life-cycle	No changes.
72–6	Aquatic organism accumulation	850.1710 850.1730 850.1850	Aquatic organisms bioavailability/ biomagnification/toxicity tests	Changed from ''conditionally required'' to ''not required'' for aquatic nonfood residential and residential outdoor uses.
72–7	Simulated or actual field testing—aquatic organisms	850.1950	Simulated or actual field testing—aquatic organisms	Changed from ''conditionally required'' to ''not required'' for aquatic nonfood residential uses. Clarified that the conditional requirement applies to turf use.

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
Subpart F—Toxicology Data Requirements				
Acute Testing				
81–1	Acute oral toxicity—rat	870.1100	Acute oral toxicity—rat	Modified test substance.
81–2	Acute dermal toxicity	870.1200	Acute dermal toxicity	Modified test substance.
81–3	Acute inhalation toxicity—rat	870.1300	Acute inhalation toxicity—rat	No changes.
81–4	Primary eye irritation—rabbit	870.2400	Primary eye irritation—rabbit	Added testing using the TGAI to support end-use products.
81–5	Primary dermal irritation	870.2500	Primary dermal irritation	Added testing using the TGAI to support end-use products.
81–6	Dermal sensitization	870.2600	Dermal sensitization	Added testing using the TGAI to support end-use products.
81–7	Acute delayed neurotoxicity—hen	870.6100	Delayed neurotoxicity (acute)—hen	No changes.
	None	870.6200	Acute neurotoxicity—rat	Replaces current neurotoxicity battery.
Subchronic Testing				
82–1	90–day Feeding—rodent	870.3100	90–day Feeding—rodent	Requirement modified to include 2 rodent species.
82–1	90–day Feeding—non-rodent	870.3150	90–day Feeding—non-rodent	No changes.
82–2	21–day Dermal	870.3200	21–day Dermal	Changed from ''conditionally required'' to ''required'' for all food uses. Not required for nonfood uses.
82–3	90–day Dermal	870.3250	90–day Dermal	Changed from ''conditionally required'' to ''required'' for all nonfood uses.
82–4	90–day Inhalation—rat	870.3465	90–day inhalation—rat	No changes.
82–5	90–day Neurotoxicity—mammal	870.6200	90–day Neurotoxicity—rat	Changed from ''conditionally required'' to ''required.''
82–5	90–day Neurotoxicity—hen	870.6100	28–day Neurotoxicity—hen	Proposed conditional requirement. Replaces 90–day neurotoxicity hen study.
Chronic Testing				
83–1	Chronic feeding—rodent and non-rodent	870.4100	Chronic feeding—rodent and non-rodent	No changes.
83–2	Oncogenicity—rat and mouse, preferred	870.4200	Carcinogenicity—rat and mouse, preferred	Changed name. Proposed requirement to perform range finding studies.
Developmental Toxicity and Reproduction				
83–3	Teratogenicity—2 species	870.3700	Prenatal developmental toxicity—rat and rabbit, preferred	Changed name. Testing required on a 2nd species for food and nonfood uses.
83–4	Reproduction—2 generation	870.3800	Reproduction	Changed from ''conditionally required'' to ''required'' for nonfood uses based on potential exposure.

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
	None	870.6300	Developmental neurotoxicity	Proposed conditional requirement. To conduct developmental neurotoxicity testing utilizing information about the chemical and its toxicity to develop a science—based approach to testing.
Mutagenicity Testing				
84–2	Gene mutation	870.5100	Bacterial reverse mutation assay	Replaces current mutagenicity battery.
84–2	Structural chromosome aberration	870.5300 870.5375	*In vitro* mammalian cell assay	Replaces current mutagenicity battery.
84–4	Other genotoxic effects	870.5385 870.5395	*In vivo* cytogenetics	Replaces current mutagenicity battery.
			Other mutagenicity studies	No changes.
Special Testing				
85–1	General metabolism	870.7485	General metabolism	No changes.
85–2	Dermal penetration	870.7600	Dermal penetration	No changes.
86–1	Domestic animal safety	870.7200	Companion animal safety	No changes.
	None	870.6500	Scheduled controlled operant behavior	Replaces current neurotoxicity battery.
	None	870.6850	Peripheral nerve function	Replaces current neurotoxicity battery.
	None	870.6855	Neurophysiology: sensory evoked potentials	Replaces current neurotoxicity battery.
	None	870.7800	Immunotoxicity	New requirement. Required for food uses and nonfood uses.
Subpart J—Nontarget Plant Protection				
121–1	Target area phytotoxicity	850.4025	Target area phytotoxicity	No changes.
Nontarget area phytotoxicity—Tier I				
122–1	Seed germination/seedling emergence	850.4200	Seed germination	Eliminated requirement.
122–1	Seed germination/Seedling emergence	850.4100	Seedling emergence	Expanded requirement to include terrestrial food and feed, aquatic food, and residential outdoor uses. Changed test substance from TGAI to TEP.
122–1	Vegetative vigor	850.4150	Vegetative vigor	Expanded requirement to include terrestrial food and feed, aquatic food, and residential outdoor uses. Changed test substance from TGAI to TEP. Eliminated requirement for data on granular and bait formulations.
122–2	Aquatic plant growth	850.4400 850.5400	Aquatic plant growth	Expanded requirement to include terrestrial food and feed, aquatic food, and residential outdoor uses.
Nontarget area phytotoxicity—Tier II				
123–1	Seed germination	850.4200	Seed germination	Eliminated requirement.

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
123–1	Seedling emergence	850.4225	Seedling emergence	Expanded conditional requirement to include terrestrial food and feed, aquatic food, and residential outdoor uses. Changed test substance from TGAI to TEP.
123–1	Vegetative vigor	850.4250	Vegetative vigor	Expanded conditional requirement to include terrestrial food and feed, aquatic food, and residential outdoor uses. Changed test substance from TGAI to TEP. Eliminated requirement for data on granular and bait formulations.
123–2	Aquatic plant growth	850.4400 850.5400	Aquatic plant growth	Expanded conditional requirement to include terrestrial food and feed, aquatic food, residential outdoor, aquatic nonfood residential, and indoor uses.
Nontarget area phytotoxicity - Tier III				
124–1	Terrestrial field	850.4300	Terrestrial field	Expanded conditional requirement to include terrestrial food and feed, aquatic food, and residential outdoor uses. Added requirement for independent method validation.
124–2	Aquatic field	850.4450	Aquatic field	Expanded conditional requirement to include terrestrial food and feed, aquatic food, and residential outdoor uses. Added requirement for independent method validation.
Subpart K—Post-application Exposure				
132–1	Foliar dissipation	875.2100	Dislodgeable foliar residue dissipation and turf transferable residues	Revised testing criteria. Expanded use sites to include testing for greenhouses, nurseries, forests, residential settings, and turf grass. Changed from ''conditionally required'' to ''required''.
132–2	Soil dissipation	875.2200	Soil residue dissipation	Revised testing criteria. Expanded use sites to include testing for greenhouses, nurseries, forests, and residential (conditionally required) settings.
	None	875.2300	Indoor surface residue dissipation	Proposed requirement. Subject to revised testing criteria.
133–3	Dermal exposure	875.2400	Dermal exposure	Revised testing criteria. Expanded use sites to include testing for greenhouses, nurseries, forests, residential settings, and turf grass. Changed from ''conditionally required'' to ''required''.
133–4	Inhalation exposure	875.2500	Inhalation exposure	Revised testing criteria. Expanded use sites to include testing for greenhouses, nurseries, forests, residential settings, golf courses, and certain indoor environments. Changed from ''conditionally required'' to ''required.''

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
	None	875.2600	Biological monitoring	Proposed conditional requirement. Subject to revised testing criteria
	None	875.2700	Product use information	Proposed requirement. Subject to revised testing criteria.
	None	875.2800	Description of human activity	Proposed requirement. Subject to revised testing criteria.
	None	875.2900	Data reporting and calculations	Proposed requirement. Subject to revised testing criteria.
	None	875.3000	Nondietary ingestion exposure	Proposed requirement for residential uses. Not required for occupational uses. Subject to revised testing criteria
Subpart N–Environmental Fate				
Degradation Testing				
161–1	Hydrolysis	835.2120	Hydrolysis	Expanded conditional requirement to include indoor food and nonfood, and residential indoor uses.
161–2	Photodegradation in water	835.2240	Photodegradation in water	Clarified conditions for when study is required.
161–3	Photodegradation on soil	835.2410	Photodegradation on soil	Changed from ''conditionally required'' to ''required'' for terrestrial food and forestry uses. Expanded requirement to include terrestrial nonfood uses.
161–4	Photodegradation in air	835.2370	Photodegradation in air	Expanded conditional requirement to include all terrestrial, greenhouse, forestry, and residential outdoor uses.
Metabolism Testing				
162–1	Aerobic soil metabolism	835.4100	Aerobic soil metabolism	New expanded conditional requirement to include aquatic uses where the pesticide is applied to aquatic sites that are intermittently dry.
162–2	Anaerobic soil metabolism	835.4200	Anaerobic soil metabolism	Reinserted. Erroneously omitted from published CFR.
162–4	Aerobic aquatic metabolism	835.4300	Aerobic aquatic metabolism	Expanded requirement to include all terrestrial and forestry uses.
162–3	Anaerobic aquatic metabolism	835.4400	Anaerobic aquatic metabolism	Expanded requirement to include all terrestrial uses.
Mobility Testing				
163–1	Leaching and adsorption/desorption	835.1230 835.1240	Leaching and adsorption/desorption	No changes.
163–2	Volatility (Lab)	835.1410	Laboratory volatility	No changes.
163–3	Volatility (Field)	835.8100	Field volatility	No changes.
Dissipation Testing				

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
164–1	Soil	835.6100	Terrestrial field dissipation	Expanded conditional requirement to include aquatic uses involving application to aquatic sites that are intermittently dry. Merged with the long-term field dissipation study. Added independent laboratory validation of methods.
164–2	Aquatic (sediment)	835.6200	Aquatic field dissipation	Expanded conditional requirement to include all terrestrial uses. Clarified conditions for when study is required. Added independent laboratory validation of methods.
164–3	Forestry	835.6300	Forestry dissipation	Changed from ''required'' to ''conditionally required.'' Added independent laboratory validation of methods.
164–4	Combination and tank mixes	835.6400	Combination and tank mixes	No changes.
164–5	Soil, long term		None	Merged with the terrestrial field dissipation study.
Accumulation Testing				
165–1	Confined rotational crops		None	Moved to Subpart O—Residue Chemistry.
165–2	Field rotational crops		None	Moved to Subpart O—Residue Chemistry.
165–3	Accumulation in irrigated crops		None	Eliminated requirement.
165–4	Accumulation in fish	850.1730	Accumulation in fish	Clarified conditions for when study is required.
165–5	Accumulation in aquatic nontarget organisms	850.1950	Accumulation in aquatic nontarget organisms	Expanded conditional requirement to include all terrestrial uses.
	None	835.7100	Ground water monitoring	Proposed conditional requirement. Added independent laboratory validation of methods.
Subpart O—Residue Chemistry				
Supporting Information				
171–2	Chemical identity	860.1100	Chemical identity	No changes.
171–3	Directions for use	860.1200	Directions for use	No changes.
171–6	Proposed tolerance	860.1550	Proposed tolerance	No changes.
171–7	Reasonable grounds in support of the petition	860.1560	Reasonable grounds in support of the petition	No changes.
171–13	Submittal of analytical reference standards	860.1650	Submittal of analytical reference standards	No changes.
Nature of the Residue				
171–4	Nature of the residue in plants	860.1300	Nature of the residue in plants	No changes.

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
171–4	Nature of the residue in animals	860.1300	Nature of the residue in animals	Clarified test substance. Expanded requirement to include: 1. Testing whenever treated crops used for feed. 2. Cases when a pesticide is applied to livestock premises or is used in livestock drinking water. Eliminated requirement for residential outdoor use.
Analytical Methods				
171–4	Residue analytical method	860.1340	Residue analytical method	Clarified test substance. Added independent laboratory validation requirement.
	None	860.1360	Multiresidue method	Previously part of the residue analytical method study.
Magnitude of the Residue Testing				
	None	860.1380	Storage stability data	Previously part of the magnitude of the residue studies.
171–4	Crop field trials	860.1500	Crop field trials	No changes.
171–4	Processed food/feed	860.1520	Processed food/feed	Clarified test substance.
171–4	Meat/milk/poultry/eggs	860.1480	Meat/milk/poultry/eggs	Clarified test substance. Clarified conditions for when study is required.
171–4	Potable water	860.1400	Potable water	Clarified test substance.
171–4	Fish	860.1400	Fish	Clarified test substance.
171–4 165–3	Irrigated crops	860.1400	Irrigated crops	Clarified test substance.
171–4	Food handling	860.1460	Food handling	No changes.
171–5	Reduction in Residues		Anticipated residues	Name change. Expanded requirement to include testing on a single serving.
165–1	Confined rotational crops	860.1850	Confined rotational crops	Moved from Environmental Fate data requirements.
165–2	Field rotational crops	860.1900	Field rotational crops	Moved from Environmental Fate data requirements. Modified conditions for when study is required.
Subpart U—Applicator Exposure				
	None	875.1100 875.1600	Dermal outdoor exposure	Proposed requirement. Subject to new testing criteria.
	None	875.1200 875.1600	Dermal indoor exposure	Proposed requirement. Subject to new testing criteria.
	None	875.1300 875.1600	Inhalation outdoor exposure	Proposed requirement. Subject to new testing criteria.
	None	875.1400 875.1600	Inhalation indoor exposure	Proposed requirement. Subject to new testing criteria.

TABLE 3.—PART 158: PROPOSED CHANGES TO DATA REQUIREMENTS[1]—Continued

Guideline No.	Current requirement	Guideline No.	Proposed requirement	Change
	None	875.1500 875.1600	Biological monitoring	Proposed conditional requirement. Subject to new testing criteria.
	None	875.1600	Data reporting and calculations	Proposed requirement. Subject to new testing criteria.
	None	875.1700	Product use information	Proposed requirement. Subject to new testing criteria.

[1] If the study requirement is not identified as a ''new requirement,'' then the change has been required on a case-by-case basis.

XXIV. Public Comments Sought

EPA invites you to provide your views on the various options as proposed, other approaches, the potential impacts of the various options (including possible unintended consequences), and any data or information that you would like the Agency to consider during the development of the final rule. In addition, the Agency welcomes specific comments on the following topics of particular interest to the Agency:

1. *Ensuring high quality data to meet EPA's mandates.* These proposed revisions to the pesticide data requirements in part 158 are intended to ensure that the Agency has the data required to support a determination of ''reasonable certainty of no harm'' under FFDCA and are an integral part of the data needed for an ''unreasonable adverse effects'' determination under FIFRA. In developing this proposed rule, EPA has evaluated its data needs to conduct the significantly expanded risk assessments required by new statutory mandates. EPA believes that this proposal describes the data needed (and only the data needed) for this purpose. The Agency welcomes your specific comments on the need for, value of, and any alternatives to, the data requirements described in this document to meet its mandates.

2. *Ensuring a sound scientific basis that is consistent with advances in scientific understanding.* These proposed revisions are intended to ensure that the data requirements in part 158 reflect current scientific understanding and scientific advances since they were issued in 1984. As discussed throughout this document, and summarized in Unit XVIII, many of these proposed revisions have been presented to, and reflect the advice and recommendations of the NRC or SAP. Issues and related materials that are brought by EPA to the SAP undergo a public review and comment opportunity before the SAP issues its report with recommendations to the Agency. The Agency welcomes your comments on the scientific basis of this proposed rule.

3. *Improving the transparency and usefulness of part 158.* Many of the revisions proposed in this document are intended to improve the usefulness of part 158 in identifying the specific data requirements that could apply to a particular pesticide application. As with the original design of part 158 in 1984, given the variety in pesticide chemistry, exposure, and hazard, these revisions are intended to retain a fair amount of flexibility in their application, while improving clarity and transparency to the regulated community. In future efforts to improve clarity and usefulness, EPA intends to issue separate revisions addressing antimicrobial pesticides, biochemical and microbial pesticides, which will highlight data requirements that apply to those pesticides. The Agency welcomes your specific comments on the Agency's efforts in this respect as described in this document and your specific suggestions for further improvements. In particular, the Agency welcomes public comment on the clarity of the proposed data requirements and the relationship between the proposed data requirements and EPA's statutory determinations.

4. *Estimating costs and benefits.* As summarized in Unit XXVII.A., the Agency has prepared a qualitative assessment of the benefits of the proposed rule, and estimates the potential annual costs to the regulated community of approximately $50 million more than current data requirements as described in part 158. The Agency believes that the costs of the rule are justified by the benefits from enhanced protection of human health and the environment. The Agency welcomes comments on its economic analysis of the proposed rule, as well as on its underlying assumptions and economic data. Describe any assumptions and provide any technical information and/or data that you used. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced. As indicated in Unit V.B.1, EPA's underlying principle in developing the proposed revisions has been to strike an appropriate balance between the need for adequate data to make the statutorily mandated determinations and informed risk management decisions, while minimizing data collection burdens on pesticide applicants. The Agency welcomes your specific comments on the Agency's efforts described in this document and your specific suggestions for further improvements.

5. *Enhancing international harmonization.* EPA is active in a number of scientific harmonization and regulatory coordination efforts through international and regional organizations, and directly with other countries, in order to develop common or compatible international approaches to pesticide review and registration. In addition, EPA has encouraged registrants to coordinate data submissions in the three NAFTA countries to facilitate joint reviews. The Agency believes that these proposed revisions reflect these efforts, and welcomes your comments on this specific point.

6. *Reducing, replacing and refining the use of animals in generating required data.* As discussed in Unit XXII, where testing is needed to develop scientifically adequate data, the Agency is committed to reducing or replacing, wherever possible, the number of animals used for testing by incorporating *in vitro* (non-animal) test methods or other alternative approaches that have been scientifically validated and have received regulatory acceptance. The Agency understands that many people remain concerned about the use of animals for research and data development purposes, and has received several requests for more expeditious adoption of alternate methods. The Agency plays an important role in the Federal interagency efforts to encourage the

reduction of the number of animals used in testing; seek opportunities to replace test methods requiring animals with alternative test methods when acceptable alternative methods are available; and refine existing test methods to optimize animal use when there is no substitute for animal testing. Recognizing the different roles of data requirements and test guidelines, the Agency welcomes your specific comments on its efforts to ensure that the data requirements continue to provide sufficient flexibility to allow for the use of alternative approaches that have been scientifically validated and have received regulatory acceptance. The Agency welcomes specific recommendations on ways to reduce the number of animals tested while still allowing the Agency to meet its statutory obligations.

XXV. References

The Agency has established an official docket for this rulemaking under Docket ID No. OPP–2004–0387. All of the documents that have been included in that docket are listed in the ''EDOCKET'' index available at *http://www.epa.gov/edocket*. Select ''Quick Search'' and then use the Docket ID No. to access the index. The following is a listing of the documents that are specifically referenced in this proposed rule. These documents, and other supporting materials, are included in the docket index. Please note that the official docket includes the documents located in the docket as well as the documents that are referenced in those documents. As indicated previously, not all docket materials are available electronically, but all publicly available docket materials are available through the Docket facility as described under **ADDRESSES**.

1. National Research Council, ''Pesticides in the Diets of Infants and Children,'' National Academy Press, Washington, D.C., 1993.

2. Mineau et al., 2001. Pesticide Acute Toxicity Reference Values for Birds, *Review of Environmental Contamination and Toxicology*, 170: 13–74.

3. U.S. Environmental Protection Agency. 1998. EPA's Contaminated Sediment Management Strategy. EPA–823–R–98–001. Office of Water, 4305, Washington, D.C. *http://www.epa.gov/waterscience/cs/stratndx.html*.

4. Bennett et al., Overview of Methods for Evaluating Effects of Pesticides on Reproduction in Birds., U.S. EPA, Environmental Research Laboratory, Corvalis, OR., EPA 600/3–91/048.

5. Bennet et al., 1990. Effects on the Duration and Timing of Dietary Methyl Parathion Exposure on Bobwhite Reproduction, *Environmental Toxicology and Chemistry*, 9: 1473–1480.

6. Bennett et al., 1991. Effects of Dietary Exposure to Methyl Parathion on Egg-laying and Incubation in Mallards, *Environmental Toxicology and Chemistry*, 10: 501–507.

7. Luster et al., 1992. Risk Assessment in Immunotoxicology I. Sensitivity and Predictability of Immune tests, *Fundam. Appl. Toxicol*, 18: 200–210.

8. Luster et al., 1993. Risk Assessment in Immunotoxicology II. Relationships Between Immune and Host Resistance Tests, *Fundamental amd Applied Toxicology*, 21: 71–82.

9. USEPA (1990) 1990 OECD Ad Hoc Meeting on Neurotoxicity Testing. Summary Report. September 1990. Eastern Research Group, MA.

10. Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Assessment. Office of Pesticide Programs, U.S. Environmental Protection Agency, Washington D.C, February, 2002.

11. FIFRA Scientific Advisory Panel. SAP Report No. 99–03, May 25, 1999 FIFRA Scientific Advisory Panel Meeting, May 25–27, 1999, held at the Sheraton Crystal City Hotel, Arlington, Virginia.

12. ILSI (2001) Developing strategies for agricultural chemical safety evaluation, a report from an April 22–23, 2001 workshop. ILSI Health and Environmental Sciences Institute. *http://hesi.ilsi.org/activities/actslist.cfm?pubentityid=8&pubactivityid=261 2001 draft*).

13. USEPA (U.S. Environmental Protection Agency), Pesticide Assessment Guidelines, Subdivision F, Hazard Evaluation: Human and Domestic Animals, Series 84, Mutagenicity, Addendum 9, Office of Pesticides and Toxic Substances, EPA–540/09–91–122, NTIS Publication No. PB91–158394, Washington, DC, 1991.

14. K. Dearfield, A. Auletta, M. Cimino and M. Moore, Considerations in the U.S. Environmental Protection Agency's testing approach for mutagenicity, Mutation Research 258 (1991) 259–283.

15. USEPA (U.S. Environmental Protection Agency), Guidelines for mutagenicity risk assessment, 51 FR 34006–34012 (1986).

16. Dourson, M.L., Knauf, L.A., and Swartout, J.C. (1972). On Reference Dose (RfD) and its underlying toxicity data base. Toxicology and Industrial Health 8:171–189.

17. Health Canada, Pesticide Management Regulatory Agency (1997) Reproductive Toxicity Testing in Proposed 40 CFR part 158, Subdivision W – Data Requirements for Antimicrobial Pesticides. November 1997 draft. Attachment to memorandum from Don Grant (PMRA) to Norm Cook/Tim McMahon/Sue Makris (USEPA/OPP), December 1, 1997.

18. Spielmann, H., and Gerbracht, U. (2001). The use of dogs as second species in regulatory testing of pesticides. Part II: subacute, subchronic and chronic studies in the dog. *Archives of Toxicology* 75(1): 1–21.

19. U. S. EPA, 2004. ''Economic Analysis of the Proposed Rule Changing Data Requirements for Conventional Pesticides,'' BEAD/OPP/USEPA, Washington, DC. Document ID No. 2004–0387–00.

XXVI. FIFRA Review Requirements

In accordance with FIFRA sec. 25(a), this proposal was submitted to the FIFRA SAP, the Secretary of Agriculture, and appropriate Congressional Committees. The SAP has waived its review of this proposal, and no comments were received from any of the Congressional Committees. USDA participated fully in the OMB interagency review process, and where warranted, changes were made to the proposal based upon its comments.

XXVII. Statutory and Executive Order Reviews

A. Executive Order 12866

Under Executive Order 12866, entitled Regulatory Planning and Review (58 FR 51735, October 4, 1993), the Office of Management and Budget (OMB) determined that this proposed rule is a ''significant regulatory action'' under sec. 3(f) of the Executive Order because this action might raise novel legal or policy issues or otherwise have a potentially significant impact on pesticide producers or registrants of pesticide products. As a result of this OMB determination, EPA submitted this proposed rulemaking to OMB for review under Executive Order 12866 and any changes made in response to OMB comments have been documented in the public docket for this rulemaking as required by sec. 6(a)(3)(E) of the Executive Order.

EPA has prepared an economic analysis of the potential costs associated with this proposed action, which is contained in a document entitled ''Economic Analysis of the Proposed Rule Changing Data Requirements for Conventional Pesticides'' (Ref. 19). A copy of this Economic Analysis is available in the public docket for this action, and is briefly summarized here.

The cost of the proposed rule is calculated as the estimated costs for the

proposed changes to the existing data requirements as currently codified in 40 CFR part 158. Since most of the data requirements contained in this proposal have been applied on a case-by-case basis over the years to reflect the evolution of scientific understanding and concerns, the Agency further categorizes the proposed revisions that are not currently codified as either newly codified (*i.e.*, data requirements that are not currently in part 158, but are, in practice, required on a case-by-case basis) or expanded existing requirements (*i.e.*, change in frequency with which a currently codified data requirement would be imposed. For example, a change from conditionally-required to required, or visa versa. Another example is a change in use pattern for an existing requirement) or newly imposed (*i.e.*, data requirement have not been previously imposed).

Using the currently codified requirements as the baseline for the impact analysis, the total annual impact to the pesticide industry is estimated to be about $51 million. Of this estimated total annual impact, about $28.9 million per year represents the cost of new data requirements that were imposed over the years but were not specified in the existing part 158, and about $21.6 million represents the cost of modified or expanded existing data requirements (*i.e.*, data requirements for certain tests and use patterns in the CFR that are changing from conditionally required (CR) to required (R)). As they have been applied to an increasing number of registrations, these data requirements have become more regularly required and are now being proposed. Included in the $51 million is about $1.9 million that is attributable to newly imposed requirements. The costs of the newly imposed requirements represents the increase costs over current practices, and therefore provide the estimated practical impact of this proposed rule to the pesticide industry.

To calculate the potential costs associated with this proposal, EPA first identified the test necessary to generate the data required, and then gathered information on the price that laboratories might charge a firm to conduct that test for the firm. We assumed that the data required would always need to be generated, but often the data are already available because the firm generated it for their own use. In such cases, the firm would simply need to submit those data to EPA, which involves less burden and cost than generating it. Some firms may have surrogate data that could be used, while others may qualify for a waiver. Both of which also involve less costs than generating the data anew. For each test identified, we averaged the low and high cost estimates provided by the various laboratories. Variations can be related to differences in the assumptions about the test performed (*e.g.*, protocol, species used), or it could simply be a difference in the price charged by the laboratory.

EPA then used historical data on pesticide registration actions that occurred over a 7 year period (1996–2002) to identify the entities that sought pesticide registration actions in the past. The data required for each registration action depends on several factors, including the type of registration action (*e.g.*, registration of a new active ingredient food use, registration of a new active ingredient non-food use, registration and amendments to registrations involving a major new use); data category or discipline (*e.g.*, toxicology, residue chemistry, human exposure), and use pattern (how the product will be used). To estimate the average incremental cost of each type of registration action, the percentage of time a particular test was required was estimated by EPA scientists, based on their past experience in the program and their involvement in developing the new data requirements.

The Agency prepared an industry profile using the same historical data on pesticide registration actions to identify the companies involved in those actions, and based it on public information gathered about those companies. EPA also used this industry profile to analyze the potential impacts of the proposed rule on small businesses, the results of which are summarized in Unit XXVII.C. The incremental costs, and a more detailed discussion of the estimating methodology employed in the analysis are presented in the economic impact analysis prepared for this proposed rule (Ref. 19).

Since the likely overall impact of this proposal on businesses is small, the Agency believes that a deleterious effect on the availability of pesticides to users is unlikely. On balance, the Agency believes that the costs of the rule are justified by the benefits from enhanced protection of human health and the environment.

The data requirements in part 158 potentially apply to new pesticides submitted for registration, to new uses of currently registered pesticides, and to existing chemicals whose databases are subject to Agency review to determine if they continue to meet registration standards. For these existing chemicals, part 158 data requirements are potentially relevant to three review programs.

Reregistration (mandated in 1988) and tolerance reassessment (mandated in 1996) are well underway. Data requirements under those programs have largely been imposed on registrants of existing chemicals, and the data have been submitted. EPA anticipates that by the time this proposed rule is promulgated, few of the data requirements will remain to be imposed for existing chemicals. Only those that are ''new'' or ''newly codified '' (*e.g.*, developmental neurotoxicity, immunotoxicity, sediment testing) have not been broadly required and may be imposed in the future under the reregistration or tolerance reassessment programs. Continued data needs for existing chemicals must be imposed under the Agency's Data Call-In (DCI) program.

Should such data be needed for reregistration or tolerance reassessment after promulgation of this rule, EPA anticipates that it will articulate the specific burden and costs associated with each DCI pursuant to the appropriate Information Collection Request (ICR) approvals under the Paperwork Reduction Act (PRA). Since the approval process for the PRA requires that EPA characterize the information collection burdens and costs incurred by registrants to comply with a DCI, a complete estimate of the burden and costs for the DCIs will be provided at that time. EPA believes that the public process associated with the PRA approval for the DCI related ICRs is a reasonable way to account for the data costs without double counting the burden. Accordingly, in this proposal EPA has not evaluated the potential burden of the proposed data requirements on registrants of existing chemicals.

A third program, registration review, mandated in 1996, requires that EPA establish a program for the periodic review of existing chemicals (goal is every 15 years). Any data requirements to be levied under that program will also be imposed under a DCI. At this time, EPA is developing a proposed rule to establish procedures for this program. An Advance Notice of Proposed Rulemaking was published in the **Federal Register** on April 26, 2000 (65 FR 24585)(FRL–6488–9).

The data requirements in this proposed rule are expected to apply to all chemicals subject to registration review (*i.e.*, all existing chemicals), depending on the conditions expressed in both final rules (this part 158 and the future registration review rule). At this time EPA has not determined how the

registration review program will function. Until the registration review program is better defined, any estimates of burden/cost will be unreliable and highly speculative. Moreover, since the requirements will also be imposed via DCIs, such burdens will also be characterized under PRA procedures described earlier.

Accordingly, EPA intends to describe generally the burden and costs of potential data requirements at the time the registration review rule is proposed, and ultimately, to more accurately and fully characterize the individual DCI burden and costs during the public process associated with PRA approval.

B. Paperwork Reduction Act (PRA)

Pursuant to the Paperwork Reduction Act (PRA), 44 U.S.C. 3501 *et seq.*, an agency may not conduct or sponsor, and a person is not required to respond to an information collection request unless it displays a currently valid OMB control number. The OMB control numbers for EPA's regulations, after appearing in the preamble of the final rule, are listed in 40 CFR part 9 and 48 CFR chapter 15, and included on the related collection instrument (*e.g.*, form or survey). Under the PRA, ''burden'' means the total time, effort, or financial resources expended by persons to generate, maintain, retain, or disclose or provide information to or for a Federal agency. This includes the time needed to review instructions; develop, acquire, install, and utilize technology and systems for the purposes of collecting, validating, and verifying information, processing and maintaining information, and disclosing and providing information; adjust the existing ways to comply with any previously applicable instructions and requirements; train personnel to be able to respond to a collection of information; search data sources; complete and review the collection of information; and transmit or otherwise disclose the information.

EPA has determined that this proposed rule imposes no significant additional information collection and paperwork burden. The information collection activity contained in this proposed rule, *i.e.*, the paperwork collection activities related to the submission of data to EPA in order to register a conventional pesticide product, are already approved by OMB under several existing ICRs. Specifically, the program activities which would generate a paperwork burden under this proposal are covered by the following ICRs:

1. The activities associated with the establishment of a tolerance are currently approved under OMB Control No. 2070–0024 (EPA ICR No. 0597);

2. The activities associated with the application for a new or amended registration of a pesticide are currently approved under OMB Control No. 2070–0060 (EPA ICR No. 0277);

3. The activities associated with the generation of data for reregistration are currently approved under OMB Control No. 2070–0107 (EPA ICR No. 1504); and

4. The activities associated with the generation of data for special review are currently approved under OMB Control No. 2070–0057 (EPA ICR No. 0922).

These existing ICRs cover the paperwork activities contained in this proposal because these activities already occur as part of the Agency's existing program activities. These program activities are an integral part of the Agency pesticide program and the corresponding ICRs will continue to be regularly renewed pursuant to the PRA. The approved burden in these ICRs were already increased in 1996 to accommodate the potential increased burden related to the implementation of the new safety standard imposed in 1996 by FQPA.

The total estimated average annual public reporting burden currently approved by OMB for these various activities ranges from 8 hours to approximately 3,000 hours per respondent, depending on the activity and other factors surrounding the particular pesticide product. Additional information about this estimate is provided in the Economic Analysis for this rulemaking.

Comments are requested on the Agency's need for this information, the accuracy of the burden estimates, and any suggested methods for minimizing respondent burden, including through the use of automated collection techniques. The Agency is particularly interested in receiving comment on the estimated testing costs and burdens that are presented in the Economic Analysis, as well as suggestions for how the Agency might best be able to provide updated and more detailed estimates in the context of the individual ICRs during the regular renewals of those ICRs every 3 years. Send comments to EPA as part of your overall comments on this proposed action in the manner specified in Unit I.C. In the final rule, the Agency will address any comments received regarding the information collection requirements contained in this proposal.

C. Regulatory Flexibility Act

Pursuant to sec. 605(b) of the Regulatory Flexibility Act (RFA), 5 U.S.C. 601 *et seq.*, the Agency hereby certifies that this proposal will not have a significant adverse economic impact on a substantial number of small entities. This determination is based on the Agency's economic analysis performed for this rulemaking, which is summarized in Unit XXVII.A., and a copy of which is available in the public docket for this rulemaking. The following is a brief summary of the factual basis for this certification.

As part of the economic analysis prepared for this rulemaking, EPA used historical data to prepare an industry profile of potentially impacted entities prepared for the economic analysis for this rulemaking, EPA determined that this proposed rule is not expected to impact any small not-for-profit organizations or small governmental jurisdictions. As such, the small entity impact analysis prepared as part of the economic analysis evaluated potentially impacted businesses that could be considered small businesses as defined by the Small Business Administration, which uses the maximum number of employees or sales for businesses in each industry sector, as that sector is defined by NAICS. For example, entities defined as Pesticide and Other Agricultural Chemical Manufacturing (325320) are considered to be a small business if they employ 500 or fewer people.

Although, as illustrated by the industry profile, the conventional pesticide industry is primarily composed of large, multi-national corporations, EPA used historical data to evaluate potential impacts on small firms that could be subject to the proposed requirements.

To determine the universe of small entities that could be subject to the proposed requirements, the Agency used workforce data to determine the size for 565 firms for which financial data had been gathered for the economic analysis. Based on that data, EPA determined that 449 qualified as small businesses using the SBA definition. Using the resulting ratio of 79%, the Agency estimated that out of the total 1804 firms in the pesticide industry, approximately 1434 firms might qualify as small and could make up the universe of small entities that could be subject to the proposed requirements.

EPA then used historical data to estimate the number of small entities potentially impacted, and the extent of that potential impact. EPA used workforce data gathered on 120 firms identified as impacted by the proposal using historical data to determine the size of 97 firms. Based on that data, we determined that 49 firms of the 97 firms (51%) qualified as small businesses.

Data was unavailable for 23 firms, but using the same ratio (51%), EPA estimated that a total of 61 small firms could be potentially impacted by the proposal. Out of the universe of 1434 small firms that could be subject to the proposed requirements, or out of the 61 small firms potentially impacted, only 35 small firms are expected to experience a cost increase representing 1% or more of gross sales, of which only 23 small firms are expected to experience a cost increase representing 3% or more of gross sales. Given these estimated impacts on small businesses, EPA has concluded that the proposed revisions will not have a significant adverse economic impact on a substantial number of small entities.

EPA is particularly interested in receiving comment from small businesses as to the benefits, costs and impacts of this proposed rule. Any comments regarding the estimated potential small entity economic impacts that this proposed regulatory action may impose on small entities should be submitted to the Agency in the manner specified in Unit I.

D. Unfunded Mandates Reform Act

Under Title II of the Unfunded Mandates Reform Act of 1995 (UMRA) (Public Law 104–4), EPA has determined that this action does not contain a Federal mandate that may result in expenditures of $100 million or more for State, local, and tribal governments, in the aggregate, or the private sector in any one year. As described in Unit XXVII.A., the annual costs associated with this action are estimated to total $51 million. This cost represents the incremental cost to applicant and registrants attributed to the additional or modified data requirements contained in this proposal. In addition, since State, local, and tribal governments are rarely a pesticide applicant or registrant, the proposed rule is not expected to significantly or uniquely affect small governments. Accordingly, this action is not subject to the requirements of secs. 202 and 205 of UMRA.

E. Executive Order 13132

Pursuant to Executive Order 13132, entitled *Federalism* (64 FR 43255, August 10, 1999), EPA has determined that this proposed rule does not have ''federalism implications,'' because it will not have substantial direct effects on the states, on the relationship between the national government and the states, or on the distribution of power and responsibilities among the various levels of government, as specified in the Order. As indicated above, instances where a state is a registrant are extremely rare. Therefore, this proposed rule may seldom affect a state government. Thus, Executive Order 13132 does not apply to this proposed rule. In the spirit of the Order, and consistent with EPA policy to promote communications between the Agency and State and local governments, EPA specifically solicits comment on this proposed rule from State and local officials.

F. Executive Order 13175

As required by Executive Order 13175, entitled *Consultation and Coordination with Indian Tribal Governments* (65 FR 67249, November 6, 2000), EPA has determined that this proposed rule does not have tribal implications because it will not have substantial direct effects on tribal governments, on the relationship between the Federal government and the Indian tribes, or on the distribution of power and responsibilities between the Federal government and Indian tribes, as specified in the Order. As indicated above, at present, no tribal governments hold, or have applied for, a pesticide registration. Thus, Executive Order 13175 does not apply to this proposed rule. In the spirit of the Order, and consistent with EPA policy to promote communications between the Agency and State and local governments, EPA specifically solicits comment on this proposed rule from tribal officials.

G. Executive Order 13045

Executive Order 13045, entitled *Protection of Children from Environmental Health Risks and Safety Risks* (62 FR 19885, April 23, 1997) does not apply to this proposed rule because this action is not designated as an ''economically significant'' regulatory action as defined by Executive Order 12866 (see Unit XXVII.A.). Further, this proposal does not establish an environmental standard that is intended to have a negatively disproportionate effect on children. To the contrary, this action will provide added protection for children from pesticide risk. The proposed data requirements are intended to address risks that, if not addressed, could have a disproportionate negative impact on children. EPA will use the data and information obtained by this proposed rule to carry out its mandate under FFDCA to give special attention to the risks of pesticides to sensitive subpopulations, especially infants and children.

H. Executive Order 13211

This rule is not subject to Executive Order 13211, entitled *Actions concerning Regulations that Significantly Affect Energy Supply, Distribution, or Use* (66 FR 28355, May 22, 2001) because it is not likely to have any significant adverse effect on the supply, distribution, or use of energy.

I. National Technology Transfer and Advancement Act

Section 12(d) of the National Technology Transfer and Advancement Act of 1995 (NTTAA), 15 U.S.C. 272 note) directs EPA to use voluntary consensus standards in its regulatory activities unless to do so would be inconsistent with applicable law or impractical. Voluntary consensus standards are technical standards (*e.g.*, materials specifications, test methods, sampling procedures, etc.) that are developed or adopted by voluntary consensus standards bodies. NTTAA directs EPA to provide Congress, through OMB, explanations when the Agency decides not to use available and applicable voluntary consensus standards. This regulation proposes the types of data to be required to support conventional pesticide registration but does not propose to require specific methods or standards to generate those data. Therefore, this proposed regulation does not impose any technical standards that would require Agency consideration of voluntary consensus standards. The Agency invites comment on its conclusion regarding the applicability of voluntary consensus standards to this rulemaking.

J. Executive Order 12898

This proposed rule does not have an adverse impact on the environmental and health conditions in low-income and minority communities. Therefore, under Executive Order 12898, entitled *Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations* (59 FR 7629, February 16, 1994), the Agency has not considered environmental justice-related issues. Although not directly impacting environmental justice-related concerns, the collection of the information contained in this proposed rule will enable the Agency to protect human health and the environment by being better able to prioritize chemical substances of concern.

List of Subjects in 40 CFR Parts 152 and 158

Administrative practice and procedure, Agricultural commodities,

Pesticides and pests, Reporting and recordkeeping requirements.

Dated: February 28, 2005.

Stephen L. Johnson,

Acting Administrator.

Therefore, it is proposed that chapter I of title 40 of the Code of Federal Regulations be amended as follows:

PART 152—[AMENDED]

1. In part 152:

a. The authority citation continues to read as follows:

Authority: 7 U.S.C. 136–136y. Subpart U is also issued under 31 U.S.C. 9701.

b. In § 152.50, by amending paragraph (f)(1) by revising the reference ''FIFRA sec. 3(c)(1)(D)'' to read ''FIFRA sec. 3(c)(1)(F),'' and by revising paragraph (f)(2) to read as follows:

§ 152.50 Contents of application.

* * * * *

(f) * * *

(2) An applicant must furnish any data specified in part 158 of this chapter that are required by the Agency to determine that the product meets the registration standard of FIFRA sec. 3(c)(5) or 3(c)(7), as applicable, and FIFRA sec. 10. An applicant may request a waiver of any data requirement by following the procedures in § 158.45 of this chapter. Each study must comply with:

(i) Section 158.32 of this chapter, with respect to format of submission.

(ii) Section 158.33 of this chapter, with respect to studies for which a claim of trade secret or confidential business information is made.

(iii) Section 158.34 of this chapter, with respect to flagging for potential adverse effects.

(iv) Section 160.12 of this chapter, with respect to a statement whether studies were conducted in accordance with Good Laboratory Practices of part 160.

* * * * *

PART 158—[AMENDED]

2. In part 158:

a. By revising the authority citation to read as follows:

Authority: 7 U.S.C. 136–136y; 21 U.S.C. 346a.

b. By revising the table of contents for part 158 to read as follows:

c. By revising subpart A to read as follows:

Subpart A—General Provisions

§ 158.1 Purpose and scope.

(a)*Purpose.* The purpose of this part is to specify the kinds of data and information EPA requires in order to make regulatory judgements under FIFRA secs. 3, 4, and 5 about the risks and benefits of pesticide products. Further, this part specifies the data and information needed to determine the safety of pesticide chemical residues under FFDCA sec. 408.

(b) *Scope.* (1) This part describes the minimum data and information EPA typically requires to support an application for pesticide registration or amendment; support the reregistration of a pesticide product; or establish or maintain a tolerance or exemption from the requirement of a tolerance for a pesticide chemical residue.

(2) This part establishes general policies and procedures associated with the submission of data in support of a pesticide regulatory action.

(3) This part does not include study protocols, methodology, or standards for conducting or reporting test results; nor does this part describe how the Agency uses or evaluates the data and information in its risk assessment and risk management decisions, or the regulatory determinations that may be based upon the data.

§ 158.3 Definitions.

All terms defined in sec. 2 of the Federal Insecticide, Fungicide, and Rodenticide Act apply to this part and are used with the meaning given in the Act. Applicable terms from the Federal Food, Drug, and Cosmetic Act also apply to this part. Individual subparts may contain definitions that pertain solely to that subpart. The following additional terms apply to this part:

Applicant means any person or entity that applies to the Agency for:

(1) An application for registration, amended registration, or reregistration

of a pesticide product under FIFRA secs. 3, 4 or 24(c).

(2) An application for an experimental use permit under FIFRA sec. 5.

(3) An application for an exemption under FIFRA sec. 18.

(4) A petition or other request for establishment or modification of a tolerance, for an exemption for the need for a tolerance, or for other clearance under FFDCA sec. 408.

(5) A submission of data in response to a notice issued by EPA under FIFRA sec. 3(c)(2)(B).

(6) Any other application, petition, or submission sent to EPA intended to persuade EPA to grant, modify, or leave unmodified a registration or other approval required as a condition of sale or distribution of a pesticide.

(7) For the purposes of this part, an applicant includes a registrant.

Registration includes a new registration, amended registration and reregistration, unless stated otherwise.

§ 158.5 Applicability.

(a) This subpart describes the data that are required to support the registration of each pesticide product. The information specified in this part must be submitted with each application for new or amended registration or for reregistration, if it has not been submitted previously or if the previously submitted information is not complete and accurate.

(b) The requirements of this part apply to the following applicants:

(1) Any person who submits an application for a new or amended registration in accordance with FIFRA sec. 3.

(2) Any person who submits an application for an experimental use permit in accordance with FIFRA sec. 5.

(3) Any person who petitions the Agency to establish, modify, or revoke a tolerance or exemption from a tolerance in accordance with FFDCA sec. 408.

(4) Any person who submits data or information to support the continuation of a registration in accordance with FIFRA sec. 3 or 4.

§ 158.30 Flexibility.

(a) FIFRA provides EPA flexibility to require, or not require, data and information for the purposes of making regulatory judgements for pesticide products. EPA maintains its authority to tailor data needs to individual pesticide chemicals. The actual data required may be modified on an individual basis to fully characterize the use and properties, characteristics, or effects of specific pesticide products under review. The Agency encourages each applicant to consult with EPA to discuss the data requirements particular to its product prior to and during the registration process.

(b) The Agency cautions applicants that the data routinely required in this part may not be sufficient to permit EPA to evaluate the potential of the product to cause unreasonable adverse effects to man or the environment. EPA may require the submission of additional data or information beyond that specified in this part if such data or information are needed to appropriately evaluate a pesticide product.

(c) This part will be updated as needed to reflect evolving program needs and advances in science.

§ 158.32 Format of data submissions.

(a) *General.* (1) The requirements of this section apply to any data submitted or cited to EPA in support of any new, pending, or existing regulatory action under FIFRA or FFDCA, including, but not limited to:

(i) Registration, amended registration or reregistration.

(ii) Experimental use permit.

(iii) Data Call-in.

(iv) Establishment, modification or revocation of a tolerance or exemption.

(v) Submission of adverse effects information under FIFRA sec. 6(a)(2).

(2) The requirements of this section do not apply to administrative materials accompanying a data submission, including forms, labeling, and correspondence.

(b) *Transmittal document.* Each submission in support of a regulatory action must be accompanied by a transmittal document, which includes:

(1) Identity of the submitter.

(2) The transmittal date.

(3) Identification of the regulatory action with which the submission is associated, *e.g.*, the registration or petition number.

(4) A list of the individual documents included in the submission.

(c) *Individual documents.* Unless otherwise specified by the Agency, each submission must be in the form of individual documents or studies. Previously submitted documents should not be resubmitted unless specifically requested by the Agency, but should be cited with adequate information to identify the previously submitted document. Each study or document should include the following:

(1) A title page including the following information:

(i) The title of the study, including identification of the substance(s) tested and the test name or data requirement addressed.

(ii) The author(s) of the study.

(iii) The date the study was completed.

(iv) If the study was performed in a laboratory, the name and address of the laboratory, project numbers or other identifying codes.

(v) If the study is a commentary on or supplement to another previously submitted study, full identification of the other study with which it should be associated in review.

(vi) If the study is a reprint of a published document, all relevant facts of publication, such as the journal title, volume, issue, inclusive page numbers, and date of publication.

(2) The appropriate statement(s) regarding any data confidentiality claims as described in § 158.33.

(3) A statement of compliance or non-compliance with respect to Good Laboratory Practice Standards as required by 40 CFR 160.12, if applicable.

(4) A complete and accurate English translation must be included for any information that is not in English.

(5) A flagging statement as prescribed by § 158.34, if applicable.

§ 158.33 Confidential data.

(a) *Definitions.* For the purposes of this section:

(1) *Registered or previously registered pesticide* means any pesticide containing an active ingredient contained in a product that is, or has ever been, an active ingredient in a product registered under sec. 3 of FIFRA. A registered pesticide that is the subject of an application for a new use falls within the category of ''registered or previously registered pesticide.''

(2) *Safety and efficacy information* means information concerning the objectives, methodology, results, or significance of any test or experiment performed on or with a registered or previously registered pesticide or its separate ingredients, impurities, or degradation products, and any information concerning the effects of such pesticide on any organism or the behavior of such pesticide in the environment, including, but not limited to, data on safety to fish and wildlife, humans and other mammals, plants, animals, and soil, and studies on persistence, translocation and fate in the environment, and metabolism.

(b) *Applicability.* (1) This section applies to information submitted pursuant to this part. It supplements the general confidentiality procedures in 40 CFR part 2, subpart B, including FIFRA confidentiality procedures at 40 CFR 2.307. To the extent that provisions in this section conflict with those in 40 CFR part 2, subpart B, the provisions in

this section take precedence. The provisions of 40 CFR 2.308 do not apply to information to which this section applies. In addition to complying with the requirements of this section, any confidentiality claims for information subject to 40 CFR part 174 (plant-incorporated protectants) must be substantiated at the time of submission as described in § 174.9 of this chapter.

(2) FFDCA sec. 408(i) protects confidential information submitted in connection with an application for a tolerance or exemption to the same extent as FIFRA sec. 10. References in this section to FIFRA sec. 10 are deemed to apply equally to information submitted pursuant to FFDCA sec. 408, pursuant to the authority in sec. 408(i).

(c) *Method of asserting business confidentiality claims*—(1) *Claim required*. Information to which this section applies (and which is submitted on or after the effective date of this regulation) will be deemed as not subject to a confidentiality claim unless a claim for that information is made in accordance with the procedures specified in this paragraph. Information not subject to a confidentiality claim may be made available to the public without further notice, subject to the requirements of FIFRA sec. 10(g).

(2) *Statement required*. Upon submission to EPA, each document must be accompanied by a signed and dated document containing one of the following statements:

(i) *Statement 1*.

No claim of confidentiality, on any basis whatsoever, is made for any information contained in this document. I acknowledge that information not designated as within the scope of FIFRA sec. 10(d)(1)(A), (B), or (C)and which pertains to a registered or previously registered pesticide is not entitled to confidential treatment and may be released to the public, subject to the provisions regarding disclosure to multinational entities under FIFRAsec. 10(g).

(ii) *Statement 2*.

Information claimed as confidential has been removed to aconfidential attachment.

No claims or markings on the document or any attachments, other than these statements and attachments submitted per in accordance with paragraph (c)(3) of this section, will be recognized as asserting a claim of confidentiality. The format of data submissions is set forth in § 158.32.

(3) *Confidential attachment*. (i) All information claimed as confidential must be submitted in a separate confidential attachment to the document and cross referenced to the specific location in the document from which it was removed. The confidential attachment must have its own title page and be paginated separately from the non-confidential document.

(ii) All information in the confidential attachment that consists of (or whose disclosure would in turn disclose) manufacturing or quality control processes must be individually identified in the confidential attachment as a claim for information within the scope of FIFRA sec. 10(d)(1)(A).

(iii) All information in the confidential attachment that consists of (or whose disclosure would in turn disclose) the details of any methods for testing, detecting, or measuring the quantity of any deliberately added inert ingredient of a pesticide, must be individually identified in the confidential attachment as a claim for information within the scope of FIFRA sec. 10(d)(1)(B).

(iv) All information in the confidential attachment that consists of (or whose disclosure would in turn disclose) the identity or percentage quantity of any deliberately added inert ingredient of a pesticide must be individually identified in the confidential attachment as a claim for information within the scope of FIFRA sec. 10(d)(1)(C).

(v) Information in the confidential attachment that is designated in accordance with paragraphs (c)(3)(ii) - (iv) of this section must be on a separate page from information that is not so designated.

(4) *Voluntary release of information to States and foreign governments.* Submitters are encouraged to include with the statement required under paragraph (c)(2) of this section the following additional statement to allow EPA to share information with State and foreign governments:

I authorize the Environmental Protection Agency to release any information contained in this document to State or foreign governments, without relinquishing proprietary rights or any confidentiality claims asserted above.

EPA will not consider such a statement to be a waiver of confidentiality or proprietary claims for the information.

(d) *Release of information*. (1) Safety and efficacy information that was submitted to EPA on or after May 4, 1988 and that has not been designated by the submitter as FIFRA sec. 10(d)(1)(A), (B), or (C) information in accordance with the applicable requirements of this section is not entitled to confidential treatment and may be disclosed to the public without further notice to the submitter, in accordance with paragraph (d)(2) of this section. Safety and efficacy information which has been designated by the submitter as FIFRA sec. 10(d)(1) (A), (B), or (C) information is entitled to confidential treatment only to the extent provided by FIFRA sec. 10(b), this section, and 40 CFR 2.208.

(2) Information that is not entitled to be protected as confidential in accordance with FIFRA sec. 10(b), this section and with EPA confidentiality regulations at 40 CFR part 2, subpart B, may be released to the public without the affirmation of non-multinational status provided under FIFRA sec. 10(g), provided that the information does not contain or consist of any complete unpublished report submitted to EPA, or excerpts or restatements of any such report which reveal the full methodology and complete results of the study, test, or experiment, and all explanatory information necessary to understand the methodology or interpret the results.

(3) Information designated as releasable to state or foreign governments in accordance with paragraph (c)(4) of this section may be released to such a government without further notice to the submitter. EPA will inform the State or foreign government of any of the confidentiality claims associated with the information.

§ 158.34 Flagging of studies for potential adverse effects.

(a) Any applicant who submits a study of a type listed in paragraph (b) of this section must submit with the study a statement in accordance with paragraph (c) of this section.

(b) The following table indicates the study types and the criteria to be applied to each. Column 1 lists the study types by name. Column 2 lists the associated Pesticide Assessment Guideline number. Column 3 lists the criteria applicable to each type of study. Column 4 lists the reporting code to be included in the statement specified in paragraph (c) of this section when any criterion is met or exceeded.

TABLE—FLAGGING CRITERIA

Study Type(s)	Guideline No.	Criteria: Treated animals show any of the following:	Criteria No.
Carcinogenicity or combined carcinogenicity/ chronic feeding study	870.4200, 870.3100, 870.3150	An incidence of neoplasms in males or females which increases with dose (positive trend p≤ 0.05); or	1
		A statistically significant (pairwise p≤ 0.05) increase of any type of neoplasm in any test group, males or females at any dose level, compared to concurrent control animals of the same sex; or	2
		An increase in any type of uncommon or rare neoplasms in any test group, males or females animals at any dose level, compared to concurrent controls of the same sex; or	3
		A decrease in the time to development of any type of neoplasms in any test group, males or females at any dose level, compared to concurrent controls of the same sex.	4
Prenatal developmental toxicity Reproduction and fertility Developmental neurotoxicity	870.3700 870.3800 870.6300	When compared to concurrent controls, treated offspring show a dose-related increase in malformations, pre- or post-natal deaths, or persistent functional or behavioral changes on a litter basis in the absence of significant maternal toxicity at the same dose level.	5
Neurotoxicity	870.6100 870.6200	When compared to concurrent controls, treated animals show a statistically or biologically significant increase in neuropathological lesions or persistent functional or behavioral changes.	6
Chronic feeding Carcinogenicity Reproduction and fertility Prenatal developmental toxicity Developmental neurotoxicity Acute or 90–day neurotoxicity	870.4100 870.4200 870.3800 870.3700 870.6300 870.6200	The no observed adverse effect level (NOAEL) from one of these studies is less than the NOAEL currently used by the Agency as the basis for either the acute or chronic reference dose.	7

(c) *Identification of studies.* For each study of a type identified in paragraph (b) of this section, the applicant (or registrant in the case of information submitted under FIFRA sec. 3(c)(2)(B)) shall include the appropriate one of the following two statements, together with the signature of the authorized representative of the company, and the date of signature:

1. *Statement 1.*

I have applied the criteria of 40 CFR 158.34 for flagging studies for potential adverse effects to the results of the attached study. This study neither meets nor exceeds any of the applicable criteria.''

2. *Statement 2.*

I have applied the criteria of 40 CFR 158.34 for flagging studies for potential adverse effects to the results of the attached study. This study meets or exceeds the criteria numbered [insert all applicable reporting codes].

§ 158.45 Waivers.

(a) The data requirements specified in this part as applicable to a category of products will not always be appropriate for every product in that category. Some products may have unusual physical, chemical, or biological properties or atypical use patterns which would make particular data requirements inappropriate, either because it would not be possible to generate the required data or because the data would not be useful in the Agency's evaluation of the risks or benefits of the product. The Agency will waive data requirements it finds are inappropriate, but will ensure that sufficient data are available to make the determinations required by the applicable statutory standards.

(b)(1) Applicants are encouraged to discuss the request with the Agency before developing and submitting supporting data, information, or other materials.

(2) All waiver requests must be submitted to the Agency in writing. The request must clearly identify the data requirement(s) for which a waiver is sought along with an explanation and supporting rationale why the applicant believes the data requirement should be waived. In addition, the applicant must describe any unsuccessful attempts to generate the required data, furnish any other information which the applicant(s) believes would support the request, and when appropriate, suggest alternative means of obtaining data to address the concern which underlies the data requirement.

(c) The Agency will review each waiver request and subsequently inform the applicant in writing of its decision. If the decision could apply to more than the requested product, the Agency, in its discretion, may choose to send a notice to all registrants or publish a notice in the **Federal Register** announcing the decision. An Agency decision denying a written request to waive a data requirement is a final Agency action.

§ 158.70 Satisfying data requirements.

(a) *General policy.* The Agency will determine whether the data submitted or cited to fulfill the data requirements specified in this part are acceptable. This determination will be based on the design and conduct of the experiment from which the data were derived, and an evaluation of whether the data fulfill the purpose(s) of the data requirement. In evaluating experimental design, the Agency will consider whether generally accepted methods were used, sufficient numbers of measurements were made to achieve statistical reliability, and sufficient controls were built into all phases of the experiment. The Agency will evaluate the conduct of each experiment in terms of whether the study was conducted in conformance

with the design, good laboratory practices were observed, and results were reproducible. The Agency will not reject data merely because they were derived from studies which, when initiated were in accordance with an Agency-recommended protocol, even if the Agency subsequently recommends a different protocol, as long as the data fulfill the purposes of the requirements as described in this paragraph.

(b) *Good laboratory practices.* Applicants must adhere to the good laboratory practice (GLP) standards described in 40 CFR part 160 when conducting studies to support the registration, amended registration or reregistration of a pesticide product. Applicants must also adhere to GLP standards when conducting a study in support of a waiver request of any data requirement which is within the scope of the GLP requirements.

(c) *Agency guidelines.* EPA has published Pesticide Assessment Guidelines that contain standards for conducting acceptable tests, guidance on the evaluation and reporting of data, definition of terms, and suggested study protocols. Copies of the Pesticide Assessment Guidelines may be obtained through the National Service Center for Environmental Publications (NSCEP), or by visiting the agency's website at *www.epa.gov/pesticides.* EPA publications can be ordered online (*www.epa.gov/ncepihom/nepishom*), or by telephone at 1–800–490–9198.

(d) *Study protocols*—(1) *General.* Any appropriate protocol may be used to generate the data required by this part, provided that it meets the purpose of the test standards specified in the pesticide assessment guidelines, and provides data of suitable quality and completeness as typified by the protocols cited in the guidelines. Applicants should use the test procedure which is most suitable for evaluation of the particular ingredient, mixture, or product. Accordingly, failure to follow a suggested protocol will not invalidate a test if another appropriate methodology is used.

(2) *Organization for Economic Cooperation and Development (OECD) protocols.* Tests conducted in accordance with the requirements and recommendations of the applicable OECD protocols can be used to develop data necessary to meet the requirements specified in this part. Applicants should note, however, that certain of the OECD recommended test standards, such as test duration and selection of test species, are less restrictive than those recommended by EPA. Therefore, when using OECD protocols, care should be taken to observe the test standards in a manner such that the data generated by the study will satisfy the requirements of this part.

(e) *Combining studies.* Certain toxicology studies may be combined to satisfy data requirements. For example, carcinogenicity studies in rats may be combined with the rat chronic toxicity study. Combining appropriate studies may be expected to reduce usage of test animals as well as reduce the cost of studies. EPA encourages this practice by including standards for acceptable combined tests in the Pesticide Assessment Guidelines. Registrants and applicants are encouraged to consider combining other tests when practical and likely to produce scientifically acceptable results. Registrants and applicants, however, must consult with the EPA before initiating combined studies.

§ 158.75 Requirements for additional data.

The data routinely required by this part may not be sufficient to permit EPA to evaluate every pesticide product. If the information required under this part is not sufficient to evaluate the potential of the product to cause unreasonable adverse effects on man or the environment, additional data requirements will be imposed. However, EPA expects that the information required by this part will be adequate in most cases for an assessment of the properties of the pesticide.

§ 158.80 Use of other data.

(a) *Data developed in foreign countries.* With certain exceptions, laboratory and field study data developed outside the United States may be submitted in support of a pesticide registration. Data generated in a foreign country which the Agency will not consider include, but are not limited to, data from tests which involved field test sites or a test material, such as a native soil, plant, or animal, that is not characteristic of the United States. Applicants submitting foreign data must take steps to assure that U.S. materials are used, or be prepared to supply data or information to demonstrate the lack of substantial or relevant differences between the selected material or test site and the U.S. material or test site. Once submitted, the Agency will determine whether or not the data meet the data requirements.

(b) *Data generated for other purposes.* Data developed for purposes other than satisfaction of FIFRA data requirements, such as monitoring studies, may also satisfy data requirements in this part. Consultation with the Agency should be arranged if applicants are unsure about suitability of such data.

d. By revising subpart B to read as follows:

Subpart B—How to Use the Data Tables

§ 158.100 Pesticide use categories.

(a) *General use categories.* There are six broad use categories used in the data tables. The six broad categories include terrestrial outdoor uses, aquatic outdoor uses, greenhouse uses, forestry uses, residential outdoor uses, and indoor uses of all types. The 6 broad use categories are further subdivided into 15 general use categories which are the basis for data requirements established by use pattern. Within the data tables, general use categories have been combined into single columns when the data requirements are the same for the combined uses. If there are no data requirements for a specific use, the column for that use is not included in the table. The 15 general use pattern groups used in the data table in this part are:

(1) Terrestrial food crop use.
(2) Terrestrial feed crop use.
(3) Terrestrial nonfood crop use.
(4) Aquatic food crop use.
(5) Aquatic nonfood residential use.
(6) Aquatic nonfood outdoor use.
(7) Aquatic nonfood industrial use.
(8) Greenhouse food crop use.
(9) Greenhouse nonfood crop use.
(10) Forestry use.
(11) Residential outdoor use.
(12) Residential indoor use.
(13) Indoor food use.
(14) Indoor nonfood use.
(15) Indoor medical use.

(b) *Use pattern index.* The Use Pattern Index is a comprehensive list of specific pesticide use patterns. The use index is alphabetized separately by site for all agricultural and all nonagricultural uses. The Use Pattern Index associates each pesticide use pattern with one or more of the 15 general use categories. It should be used in conjunction with the data tables to determine the applicability of data requirements to specific uses. The Pesticide Use Pattern Index, which will be updated periodically, is available from the Agency or may be obtained from the Agency's website at *http://www.epa.gov/pesticides.*

(c) Applicants unsure of the correct use category for their particular product should consult the Agency.

§ 158.110 Required and conditionally required data.

Some data and information specified in this part are required (R) for the evaluation of some or all types of products. However, other data and

information specified as conditionally required (CR) are required only if the product's pattern of use, results of other tests, or other pertinent factors meet the criteria specified in those sections.

(a) Data designated as ''required'' (R) for products with a given use pattern are required by EPA to evaluate the risks or benefits of a product having that use pattern. Further clarification of the applicability of the data requirement often is located in the test notes accompanying the table.

(b) Data designated as ''conditionally required'' (CR) for products with a given use pattern are required by EPA to evaluate the risks or benefits of a product having that use pattern if the product meets the conditions specified in the notes accompanying the requirement. The determination of whether the data must be submitted is based on the product's use pattern, physical or chemical properties, expected exposure of nontarget organisms, and/or results of previous testing (for example, tier testing). Applicants must evaluate each applicable test note for the conditions and criteria to be considered in determining whether conditionally required data must be submitted.

§ 158.120 Determining data requirements.

As with current practice, the actual data and studies required may be modified on an individual basis to fully characterize the use and properties of specific pesticide products under review. While EPA is attempting to assist the applicant in this subpart, it is important to emphasize that it is the applicant's obligation under FIFRA to demonstrate that an individual product meets the standard under FIFRA and/or FFDCA. Accordingly, applicants are encouraged to consult with the Agency on the appropriate data requirements as set forth here as they relate to their specific product prior to and during the registration process.

(a) *Finding the appropriate data table.* (1) Pesticide data requirements for conventional chemical active ingredients and related substances are presented in subparts D, E, F, G, J, K, N, O, and U of this part in the form of a series of data tables, each addressing a particular scientific discipline or data topic. Data requirements for biochemical and microbial pest control agents are contained and are described separately within subparts L and M of this part, respectively.

(2) Key to table notations. R = required data; CR = conditionally required data; NR = Not required; MP = manufacturing-use product; EP = end-use product; TEP = typical end-use product; TGAI = technical grade of the active ingredient; PAI = ''pure'' active ingredient; PAIRA = ''pure'' active ingredient, radiolabeled; Choice = choice of several test substances depending on studies required. Brackets indicate which data requirements also apply to experimental use permits (EUPS).

(b) *Identifying required studies.* To determine the specific kinds of data needed to support the registration use of each pesticide product, the applicant should:

(1) Refer to the applicable subpart(s) of this part. These subparts describe the data requirements including data tables for each subject area.

(2) Select the general use pattern(s) that best covers the use pattern(s) specified on the pesticide product label as explained in § 158.100. All applicable use patterns must be included.

(3) Proceed down the appropriate general use pattern column in the table and note which tests are required (R), conditionally required (CR), or not required (NR). Required and conditionally required studies are described in § 158.110.

(4) Review the notes for each requirement to determine its applicability to the specific product proposed for registration.

(5)(i) Proceed down the Test substance columns and determine the appropriate test substance needed for that study. For toxicology studies, if the data are intended to support a manufacturing-use product, use the first column. If the data are intended to support an end-use product, use the information listed in the second column.

(ii) The test substances columns specify which substance is to be subjected to testing. Applicants should note that the substance that should be used when performing the study may or may not be the product itself. For example, the data from a certain study may be required to support the registration of an end-use product, but the test substance column may state that the particular test shall be performed using the technical grade of the active ingredient(s) in the end-use product.

(iii) Manufacturing-use products (MP) and end-use products (EP) containing a single active ingredient and no intentionally added inert ingredients are considered identical in composition to each other, and to the technical grade of the active ingredient (TGAI) from which they were derived. Therefore, the data from a test conducted using any one of these as the test substance is also suitable to meet the requirement (if any) for the same test to be conducted using either of the other substances.

(6) Refer to the Pesticide Assessment Guideline reference number for each study located in the last column. See § 158.70(c) for information pertaining to the guidelines and how to obtain copies.

§ 158.130 Purposes of the registration data requirements.

(a) *General.* The data requirements for registration are intended to generate data and information necessary to address concerns pertaining to the identity, composition, potential adverse effects and environmental fate of each pesticide.

(b) [Reserved].

(c) *Residue chemistry.* (1) Residue chemistry data 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 food or feed.

(2) Information on the chemical identity and composition of the pesticide product, the amounts, frequency and time of the pesticide application, and results of test on the amount of residues remaining on or in the treated food or feed, are needed to support a finding as to the magnitude and identity of residues which result in food or animal feed as a consequence of a proposed pesticide usage.

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

(d) *Environmental fate*—(1) *General.* The data generated by environmental fate studies are used to: assess the toxicity to man through exposure of humans to pesticide residues remaining after application, either upon reentering treated areas or from consuming inadvertantly-contaminated food; assess the presence of widely distributed and persistent pesticides in the environment which may result in loss of usable land, surface water, ground water, and wildlife resources; and, assess the potential environmental exposure of other nontarget organisms, such as fish and wildlife, to pesticides. Another specific purpose of the environmental fate data requirements is to help applicants and the Agency estimate expected environmental concentrations of pesticides in specific habitats where threatened or endangered species or other wildlife populations at risk are found.

(2) *Degradation studies.* The data from hydrolysis and photolysis studies are used to determine the rate of pesticide degradation and to identify pesticides

that may adversely affect nontarget organisms.

(3) *Metabolism studies.* Data generated from aerobic and anaerobic metabolism studies are used to determine the nature and availability of pesticides to rotational crops and to aid in the evaluation of the persistence of a pesticide.

(4) *Mobility studies.* These data requirements pertain to leaching, adsorption/desorption, and volatility of pesticides. They provide information on the mode of transport and eventual destination of the pesticide in the environment. This information is used to assess potential environmental hazards related to: contamination of human and animal food; loss of usable land and water resources to man through contamination of water (including ground water); and habitat loss of wildlife resulting from pesticide residue movement or transport in the environment.

(5) *Dissipation studies.* The data generated from dissipation studies are used to assess potential environmental hazards (under actual field use conditions) related to: reentry into treated areas; hazards from residues in rotational crops and other food sources; and the loss of land as well as surface and ground water resources.

(6) *Accumulation studies.* Accumulation studies indicate pesticide residue levels in food supplies that originate from wild sources or from rotational crops. Rotational crop studies are necessary to establish realistic crop rotation restrictions and to determine if tolerances may be needed for residues on rotational crops. Data from irrigated crop studies are used to determine the amount of pesticide residues that could be taken up by representative crops irrigated with water containing pesticide residues. These studies allow the Agency to establish label restrictions regarding application of pesticides on sites where the residues can be taken up by irrigated crops. These data also provide information that aids the Agency in establishing any corresponding tolerances that would be needed for residues on such crops. Data from pesticides accumulation studies in fish are used to establish label restrictions to prevent applications in certain sites so that there will be minimal residues entering edible fish or shell fish. These residue data are also used to determine if a tolerance or action level is needed for residues in aquatic animals eaten by humans.

(e) *Hazards to humans and domestic animals.* Data required to assess hazards to humans and domestic animals are derived from a variety of acute, subchronic and chronic toxicity tests, and tests to assess mutagenicity and pesticide metabolism.

(1) *Acute studies.* Determination of acute oral, dermal and inhalation toxicity is usually the initial step in the assessment and evaluation of the toxic characteristics of a pesticide. These data provide information on health hazards likely to arise soon after, and as a result of, short-term exposure. Data from acute studies serve as a basis for classification and precautionary labeling. For example, acute toxicity data are used to calculate farmworker reentry intervals and to develop precautionary label statements pertaining to protective clothing requirements for applicators. They also provide information used in establishing the appropriate dose levels in subchronic and other studies; provide initial information on the mode of toxic action(s) of a substance; and determine the need for child resistant packaging. Information derived from primary eye and primary dermal irritation studies serves to identify possible hazards from exposure of the eyes, associated mucous membranes and skin.

(2) *Subchronic studies.* Subchronic tests provide information on health hazards that may arise from repeated exposures over a limited period of time. They provide information on target organs and accumulation potential. The resulting data are also useful in selecting dose levels for chronic studies and for establishing safety criteria for human exposure. These tests are not capable of detecting those effects that have a long latency period for expression (*e.g.*, carcinogenicity).

(3) *Chronic studies.* Chronic toxicity (usually conducted by feeding the test substance to the test species) studies are intended to determine the effects of a substance in a mammalian species following prolonged and repeated exposure. Under the conditions of this test, effects which have a long latency period or are cumulative should be detected. The purpose of long-term oncogenicity studies is to observe test animals over most of their life span for the development of neoplastic lesions during or after exposure to various doses of a test substance by an appropriate route of administration.

(4) *Developmental toxicity and reproduction studies.* The developmental toxicity study is designed to determine the potential of the test substance to induce structural and/or other abnormalities to the fetus as the result of exposure of the mother during pregnancy. Two-generation reproduction testing is designed to provide information concerning the general effects of a test substance on gonadal function, estrus cycles, mating behavior, conception, parturition, lactation, weaning, and the growth and development of the offspring. The study may also provide information about the effects of the test substance on neonatal morbidity, mortality, and preliminary data on teratogenesis and serve as a guide for subsequent tests.

(5) *Mutagenicity studies.* For each test substance a battery of tests are required to assess potential to affect the mammalian cell's genetic components. The objectives underlying the selection of a battery of tests for mutagenicity assessment are:

(i) To detect, with sensitive assay methods, the capacity of a chemical to alter genetic material in cells.

(ii) To determine the relevance of these mutagenic changes to mammals.

(iii) When mutagenic potential is demonstrated, to incorporate these findings in the assessment of heritable effects, oncogenicity, and possibly, other health effects.

(6) *Metabolism studies.* Data from studies on the absorption, distribution, excretion, and metabolism of a pesticide aid in the valuation of test results from other toxicity studies and in the extrapolation of data from animals to man. The main purpose of metabolism studies is to produce data which increase the Agency's understanding of the behavior of the chemical in its consideration of the human exposure anticipated from intended uses of the pesticide.

(f) *Applicator and post-application exposure.* Data are used to evaluate exposures to persons in occupational and non-occupational settings, including agricultural, residential, commercial, institutional and recreational sites. Data include oral, dermal and inhalation exposure data, post-application residue data, post-application monitoring data, use information, and human activity information. These data, together with toxicology data, are used to determine whether application or post-application risks are of concern, and, where appropriate, to develop post-application restrictions such as reentry restrictions.

(g) *Pesticide spray drift evaluation.* Data required to evaluate pesticide spray drift are derived from studies of droplet size spectrum and spray drift field evaluations. These data contribute to the development of the overall exposure estimate and, along with data on toxicity for humans, fish and wildlife, or plants, are used to assess the potential hazard of pesticides to these organisms. A purpose common to all these tests is to provide data which will be used to determine the need for (and

appropriate wording for) precautionary labeling to minimize the potential adverse effect to nontarget organisms.

(h) *Hazards to nontarget organisms*—(1) *General*. The information required to assess hazards to nontarget organisms are derived from tests to determine pesticidal effects on birds, mammals, fish, terrestrial and aquatic invertebrates and plants. These tests include short-term acute, subacute, reproduction, simulated field, and full field studies arranged in a hierarchial or tier system which progresses from the basic laboratory tests to the applied field tests. The results of each tier of test must be evaluated to determine the potential of the pesticide to cause adverse effects, and to determine whether further testing is required. A purpose common to all data requirements is to provide data which determines the need for (and appropriate wording for) precautionary label statements to minimize the potential adverse effects to nontarget organisms.

(2) *Short-term studies*. The short-term acute and subchronic laboratory studies provide basic toxicity information which serves as a starting point for the hazard assessment. These data are used: to establish acute toxicity levels of the active ingredient to the test organisms; to compare toxicity information with measured or estimated pesticide residues in the environment in order to assess potential impacts on fish, wildlife and other nontarget organisms; and to indicate whether further laboratory and/or field studies are needed.

(3) *Long-term and field studies*. Additional studies (*i.e.*, avian, fish, and invertebrate reproduction, lifecycle studies and plant field studies) may be required when basic data and environmental conditions suggest possible problems. Data from these studies are used to: estimate the potential for chronic effects, taking into account the measured or estimated residues in the environment; and to determine if additional field or laboratory data are necessary to further evaluate hazards. Simulated field and/or field data are used to examine acute and chronic adverse effects on captive or monitored fish and wildlife populations under natural or near-natural environments. Such studies are required only when predictions as to possible adverse effects in less extensive studies cannot be made, or when the potential for adverse effects is high.

(i) *Product performance*. Requirements to develop data on product performance provide a mechanism to ensure that pesticide products will control the pests listed on the label and that unnecessary pesticide exposure to the environment will not occur as a result of the use of ineffective products. Specific performance standards are used to validate the efficacy data in the public health areas, including disinfectants used to control microorganisms infectious to man in any area of the inanimate environment and those pesticides used to control vertebrates (such as rodents, birds, bats and skunks) that may directly or indirectly transmit diseases to humans.

Subpart C [Removed and Reserved]

e. By removing and reserving subpart C.

f. By revising subpart D to read as follows:

Subpart D—Product Chemistry

§ 158.300 Definitions.

The following terms are defined for the purposes of this subpart:

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, defoliant, or nitrogen stabilizer, within the meaning of FIFRA sec. 2(b).

End-use product means a pesticide product whose labeling: (1) 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 growth of plants, or as a nitrogen stabilizer, and (2) does not state that the product may be used to manufacture or formulate other pesticide products.

Formulation means: (1) 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, or (2) the repackaging of any registered product.

Impurity means 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.

Impurity associated with an active ingredient means: (1) Any impurity present in the technical grade of active ingredient; and (2) any impurity which forms in the 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 the active ingredient, which is intentionally included in a pesticide product.

Integrated system means a process for producing a pesticide product that: (1) Contains any active ingredient derived from a source that is not an EPA-registered product; or (2) contains any active ingredient that was produced or acquired in a manner that does not permit its inspection by the Agency under FIFRA sec. 9(a) prior to its use in the process.

Manufacturing-use product means any pesticide product other than an end-use product. A product may consist of the technical grade of active ingredient only, or may contain inert ingredients, such as stabilizers or solvents.

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.

Starting material means a substance used to synthesize or purify a technical grade of active ingredient (or the practical equivalent of the technical grade ingredient if the technical grade cannot be isolated) by chemical reaction.

Technical grade of active ingredient means a material containing an active ingredient: (1) Which contains no inert ingredient, other than one used for purification of the active ingredient; and (2) which is produced on a commercial or pilot plant production scale (whether or not it is ever held for sale).

§ 158.310 Product chemistry data requirements table.

(a) *General*. (1) Sections 158.100 through 158.130 describe how to use this table to determine the product chemistry data requirements for a particular pesticide product. Notes that apply to an individual test and include specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (f) of the section.

(2) Depending on the results of the required product chemistry studies, appropriate use restrictions, labeling requirements, or special packaging requirements may be imposed.

(3) All product chemistry data, as described in this section, are required to be submitted to support a request for an experimental use permit.

(b) *Use patterns*. Product chemistry data are required for all pesticide products and are not use specific.

(c) *Test substance*. Data requirements that list only the manufacturing-use product as the test substance apply to

products containing solely the technical grade of the active ingredient and manufacturing-use products to which other ingredients have been intentionally added.

(d) *Key*. R=Required; CR=Conditionally required; MP=Manufacturing-use product; NR=Not required; EP=End-use product; TGAI=Technical grade of the active ingredient; PAI=Pure active ingredient.

(e) *Table*. The following table shows the data requirements for product chemistry. The table notes are shown in paragraph (f) of this section.

PRODUCT CHEMISTRY DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Pattern	Test substance to support		Test Note No.
		All	MP	EP	
Product Identity and Composition					
830.1550	Product identity and composition	R	MP	EP	1
830.1600	Description of materials used to produce the product	R	MP	EP	2
830.1620	Description of production process	R	MP	EP	3
830.1650	Description of formulation process	R	MP	EP	4
830.1670	Discussion of formulation of impurities	R	MP, and possibly TGAI	EP, and possibly TGAI	5
830.1700	Preliminary analysis	CR	MP, and possibly TGAI	EP, and possibly TGAI	6, 9, 10
830.1750	Certified limits	R	MP	EP	7
830.1800	Enforcement analytical method	R	MP	EP	8
830.1900	Submittal of samples	CR	MP, PAI and TGAI	EP, PAI, TGAI	9, 11
Physical and Chemical Properties.					
830.6302	Color	R	MP and TGAI	TGAI	9
830.6303	Physical state	R	MP and TGAI	EP and TGAI	9
830.6304	Odor	R	MP and TGAI	TGAI	9
830.6313	Stability to normal and elevated temperatures, metals, and metal ions	R	TGAI	TGAI	9, 12
830.6314	Oxidation/reduction: chemical incompatability	CR	MP	EP	13
830.6315	Flammability	CR	MP	EP	14
830.6316	Explodability	CR	MP	EP	15
830.6317	Storage stability	R	MP	EP	
830.6319	Miscibility	CR	MP	EP	16
830.6320	Corrosion characteristics	R	MP	EP	
830.6321	Dielectric breakdown voltage	CR	NR	EP	17
830.7000	pH	CR	MP and TGAI	EP and TGAI	9, 18
830.7050	UV/visible light absorption	R	TGAI	TGAI	
830.7100	Viscosity	CR	MP	EP	19
830.7200	Melting point/melting range	R	TGAI or PAI	TGAI or PAI	9, 20
830.7220	Boiling point/boiling range	R	TGAI or PAI	TGAI or PA	9, 21
830.7300	Density/relative density/bulk density	R	MP and TGAI	EP and TGAI	9, 22
830.7370	Dissociation constants in water	R	TGAI or PAI	TGAI or PAI	9, 23
830.7520	Particle size, fiber length, and diameter distribution	CR	TGAI or PAI	TGAI or PAI	24

PRODUCT CHEMISTRY DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Pattern	Test substance to support		Test Note No.
		All	MP	EP	
830.7550 830.7560 830.7570	Partition coefficient (n-octanol/water)	CR	TGAI or PAI	TGAI or PAI	25
830.7840 830.7860	Water solubility	R	TGAI or PAI	TGAI or PAI	9
830.7950	Vapor pressure	R	TGAI or PAI	TGAI or PAI	9, 26

(f) *Test notes.* The following test notes are applicable to the product chemistry data requirements in the table to paragrpah (e) of this section:

1. Data must be provided in accordance with § 158.320.
2. Data must be provided in accordance with § 158.325.
3. Data must be provided in accordance with § 158.330.
4. Data must be provided in accordance with § 158.335.
5. Data must be provided in accordance with § 158.340.
6. Data must be provided in accordance with § 158.345.
7. Data must be provided in accordance with § 158.350.
8. Data must be provided in accordance with § 158.355.
9. If the TGAI cannot be isolated, data are required on the practical equivalent of the TGAI.
10. Data are required if the product is produced by an integrated system.
11. Basic manufacturers are required to provide the Agency with a sample of each TGAI used to formulate a product produced by an integrated system when the new TGAI is first used as a formulating ingredient in products registered under FIFRA. A sample of the active ingredient (PAI) suitable for use as an analytical standard is also required at this time. Samples of end-use products produced by an integrated system must be submitted on a case-by-case basis.
12. Data on the stability to metals and metal ions is required only if the active ingredient is expected to come in contact with either material during storage.
13. Required when the product contains an oxidizing or reducing agent.
14. Required when the product contains combustible liquids.
15. Required when the product is potentially explosive.
16. Required when the product is an emulsifiable liquid and is to be diluted with petroleum solvent.
17. Required when the EP is a liquid and is to be used around electrical equipment.
18. Required when the test substance is soluble or dispersible in water.
19. Required when the product is a liquid.
20. Required when the TGAI is solid at room temperature.
21. Required when the TGAI is liquid at room temperature.
22. True density or specific density are required for all test substances. Data on bulk density is required for MPs that are solid at room temperature.
23. Required when the test substance contains an acid or base functionality (organic or inorganic) or an alcoholic functionality (organic).
24. Required for water insoluble test substances ($<10^{-6}$ g/l) and fibrous test substances with diameter ≥0.1 μm.
25. Required for all organic chemicals unless they dissociate in water or are partially or completely soluble in water.
26. Not required for salts.

§ 158.320 Product identity and composition.

Information on the composition of the pesticide product must be furnished. The information required by paragraphs (a), (b), and (f) of this section must be provided for each product. In addition, if the product contains is produced by an integrated system, the information on impurities required by paragraphs (c) and (d) of this section must be provided.

(a) *Active ingredient.* The following information is required for each active ingredient in the product:

(1) If the source of any active ingredient in the product is an EPA-registered product:

(i) The chemical and common name (if any) of the active ingredient, as listed on the source product.

(ii) The nominal concentration of the active ingredient in the product, based upon the nominal concentration of active ingredient in the source product.

(iii) Upper and lower certified limits of the active ingredient in the product, in accordance with § 158.350.

(2) If the source of any active ingredient in the product is not an EPA-registered product:

(i) The chemical name according to Chemical Abstracts Society (CAS) nomenclature, the CAS Registry Number, and any common names.

(ii) The molecular, structural, and empirical formulae and the molecular weight or weight range.

(iii) The nominal concentration.

(iv) Upper and lower certified limits of the active ingredient in accordance with § 158.350.

(v) The purpose of the ingredient in the formulation.

(b) *Inert ingredients.* The following information is required for each inert ingredient (if any) in the product:

(1) The chemical name of the ingredient according to Chemical Abstracts Society nomenclature, the CAS Registry Number, and any common names (if known). If the chemical identity or chemical composition of an ingredient is not known to the applicant because it is proprietary or trade secret information, the applicant must ensure that the supplier or producer of the ingredient submits to the Agency (or has on file with the Agency) information on the identity or chemical composition of the ingredient. Generally, it is not required that an applicant know the identity of each ingredient in a mixture that he uses in his product. However, in certain circumstances, the Agency may require that the applicant know the identity of a specific ingredient in such a mixture. If the Agency requires specific knowledge of an ingredient, it will notify the applicant in writing.

(2) The nominal concentration in the product.

(3) Upper and lower certified limits in accordance with § 158.350.

(4) The purpose of the ingredient in the formulation.

(c) *Impurities of toxicological significance associated with the active ingredient.* For each impurity associated with the active ingredient that is determined by EPA to be toxicologically significant, the following information is required:

(1) Identification of the ingredient as an impurity.

(2) The chemical name of the impurity.

(3) The nominal concentration of the impurity in the product.

(4) A certified upper limit, in accordance with § 158.350.

(d) *Other impurities associated with the active ingredient.* For each other impurity associated with an active ingredient that was found to be present in any sample at a level ≥0.1 percent by

weight of the technical grade active ingredient the following information is required:

(1) Identification of the ingredient as an impurity.

(2) The chemical name of the impurity.

(3) The nominal concentration of the impurity in the final product.

(e) *Impurities associated with an inert ingredient.* [Reserved]

(f) *Ingredients that cannot be characterized.* If the identity of any ingredient or impurity cannot be specified as a discrete chemical substance (such as mixtures that cannot be characterized or isomer mixtures), the applicant must provide sufficient information to enable EPA to identify its source and qualitative composition.

§ 158.325 Description of materials used to produce the product.

The following information must be submitted on the materials used to produce the product:

(a) *Products not produced by an integrated system.* (1) For each active ingredient that is derived from an EPA-registered product:

(i) The name of the EPA-registered product.

(ii) The EPA registration number of that product.

(2) For each inert ingredient:

(i) Each brand name, trade name, common name, or other commercial designation of the ingredient.

(ii) All information that the applicant knows (or that is reasonably available to him) concerning the composition (and, if requested by the Agency, chemical and physical properties) of the ingredient, including a copy of technical specifications, data sheets, or other documents describing the ingredient.

(iii) If requested by the Agency, the name and address of the producer of the ingredient or, if that information is not known to the applicant, the name and address of the supplier of the ingredient.

(b) *Products produced by an integrated system.* (1) The information required by paragraph (a)(1) of this section concerning each active ingredient that is derived from an EPA-registered product (if any).

(2) The following information concerning each active ingredient that is not derived from an EPA-registered product:

(i) The name and address of the producer of the ingredient (if different from the applicant).

(ii) Information about each starting material used to produce the active ingredient, as follows:

(A) Each brand name, trade name, or other commercial designation of the starting material.

(B) The name and address of the person who produces the starting material or, if that information is not known to the applicant, the name and address of each person who supplies the starting material.

(C) All information that the applicant knows (or that is reasonably available to him), concerning the composition (and if requested by the Agency, chemical or physical properties) of the starting material, including a copy of all technical specifications, data sheets, or other documents describing it.

(3) The information required by paragraph (a)(2) of this section concerning each inert ingredient.

(c) *Additional information.* On a case-by-case basis, the Agency may require additional information on substances used in the production of the product.

§ 158.330 Description of production process.

If the product is produced by an integrated system, the applicant must submit information on the production (reaction) processes used to produce the active ingredients in the product. The applicant must also submit information about the formulation process, in accordance with § 158.335.

(a) Information must be submitted for the current production process for each active ingredient that is not derived from an EPA-registered product. If the production process is not continuous (a single reaction process form starting materials to active ingredient), but is accomplished in stages or by different producers, the information must be provided for each such production process.

(b) The following information must be provided for each process resulting in a separately isolated substance:

(1) The name and address of the producer who uses the process, if not the same as the applicant.

(2) A general characterization of the process (*e.g.*, whether it is a batch or continuous process).

(3) A flow chart of the chemical equations of each intended reaction occurring at each step of the process, and of the duration of each step and of the entire process.

(4) The identity of the materials used to produce the product, their relative amounts, and the order in which they are added.

(5) A description of the equipment used that may influence the composition of the substance produced.

(6) A description of the conditions (*e.g.*, temperature, pressure, pH, humidity) that are controlled during each step of the process to affect the composition of the substance produced, and the limits that are maintained.

(7) A description of any purification procedures (including procedures to recover or recycle starting materials, intermediates or the substance produced).

(8) A description of the procedures used to assure consistent composition of the substance produced, *e.g.*, calibration of equipment, sampling regimens, analytical methods, and other quality control methods.

§ 158.335 Description of formulation process.

The applicant must provide information on the formulation process of the product (unless the product consists solely of a technical grade of active ingredient) as required by the following sections:

(a) Section 158.330(b)(2), pertaining to characterization of the process.

(b) Section 158.330(b)(4), pertaining to ingredients used in the process.

(c) Section 158.330(b)(5), pertaining to process equipment.

(d) Section 158.330(b)(6), pertaining to the conditions of the process.

(e) Section 158.330(b)(8), pertaining to quality control measures.

§ 158.340 Discussion of formation of impurities.

The applicant must provide a discussion of the impurities that may be present in the product, and why they may be present. The discussion should be based on established chemical theory and on what the applicant knows about the starting materials, technical grade of active ingredient, inert ingredients, and production or formulation process. If the applicant has reason to believe that an impurity that EPA would consider toxicologically significant may be present, the discussion must include an expanded discussion of the possible formation of the impurity and the amounts at which it might be present. The impurities which must also be discussed are the following, as applicable:

(a) *Technical grade active ingredients and products produced by an integrated system.* (1) Each impurity associated with the active ingredient which was found to be present in any analysis of the product conducted by or for the applicant.

(2) Each other impurity which the registrant or applicant has reason to believe may be present in his product at any time before use at a level ≥0.1 percent (1,000 ppm) by weight of the technical grade of the active ingredient, based on what he knows about the following:

(i) The composition (or composition range) of each starting material used to produce his product.

(ii) The impurities which the applicant knows are present (or believes are likely to be present) in the starting materials, and the known or presumed level (or range of levels) of these impurities.

(iii) The intended reactions and side reactions which may occur in the production of the product, and the relative amounts of byproduct impurities produced by such reactions.

(iv) The possible degradation of the ingredients in the product after its production but prior to its use.

(v) Post-production reactions between the ingredients in the product.

(vi) The possible migration of components of packaging materials into the pesticide.

(vii) The possible carryover of contaminants from use of production equipment previously used to produce other products or substances.

(viii) The process control, purification and quality control measures used to produce the product.

(b) *Products not produced by an integrated system.* Each impurity associated with the active ingredient which the applicant has reason to believe may be present in the product at any time before use at a level ≥0.1 percent (1,000 ppm) by weight of the product based on what he knows about the following:

(1) The possible carryover of impurities present in any registered product which serves as the source of any of the product's active ingredients. The identity and level of impurities in the registered source need not be discussed or quantified unless known to the formulator.

(2) The possible carryover of impurities present in the inert ingredients in the product.

(3) Possible reactions occurring during the formulation of the product between any of its active ingredients, between the active ingredients and inert ingredients, or between the active ingredient and the production equipment.

(4) Post-production reactions between any of the product's active ingredients and any other component of the product or its packaging.

(5) Possible migration of packaging materials into the product.

(6) Possible contaminants resulting from earlier use of equipment to produce other products.

(c) *Expanded discussion.* On a case-by-case basis, the Agency may require an expanded discussion of information of impurities:

(1) From other possible chemical reactions.

(2) Involving other ingredients.

(3) At additional points in the production or formulation process.

§ 158.345 Preliminary analysis.

(a) If the product is produced by an integrated system, the applicant must provide a preliminary analysis of each technical grade of active ingredient contained in the product to identify all impurities present at 0. 1 percent or greater of the technical grade of the active ingredient. The preliminary analysis should be conducted at the point in the production process after which no further chemical reactions designed to produce or purify the substances are intended.

(b) Based on the preliminary analysis, a statement of the composition of the technical grade of the active ingredient must be provided. If the technical grade of the active ingredient cannot be isolated, a statement of the composition of the practical equivalent of the technical grade of the active ingredient must be submitted.

§ 158.350 Certified limits.

The applicant must propose certified limits for the ingredients in the product. Certified limits become legally binding limits upon approval of the application. Certified limits will apply to the product from the date of production to date of use, unless the product label bears a statement prohibiting use after a certain date, in which case the certified limits will apply only until that date.

(a) *Ingredients for which certified limits are required.* Certified limits are required on the following ingredients of a pesticide product:

(1) An upper and lower limit for each active ingredient.

(2) An upper and lower limit for each inert ingredient.

(3) If the product is a technical grade of active ingredient or is produced by an integrated system, an upper limit for each impurity of toxicological significance associated with the active ingredient and found to be present in any sample of the product.

(4) On a case-by-case basis, certified limits for other ingredients or impurities as specified by EPA.

(b) *EPA determination of standard certified limits for active and inert ingredients.* (1) Unless the applicant proposes different limits as provided in paragraph (c) of this section, the upper and lower certified limits for active and inert ingredients will be determined by EPA. EPA will calculate the certified limits on the basis of the nominal concentration of the ingredient in the product, according to the table in paragraph (b)(2) of this section.

(2) Table of standard certified limits.

STANDARD CERTIFIED LIMITS

If the nominal concentration (N) for the ingredient and percentage by weight for the ingredient is:	The certified limits for that ingredient will be as follows:	
	Upper Limit	Lower Limit
N ≤1.0%	N + 10%N	N - 10%N
1.0% ≤N ≤20.0%	N + 5%N	N - 5%N
20.0%≤N≤100.0%	N + 3%N	N - 3%N

(c) *Applicant proposed limits.* (1) The applicant may propose a certified limit for an active or inert ingredient that differs from the standard certified limit calculated according to paragraph (b)(2) of this section.

(2) If certified limits are required for impurities, the applicants must propose a certified limit. The standard certified limits may not be used for such substances.

(3) Certified limits should:

(i) Be based on a consideration of the variability of the concentration of the ingredient in the product when good manufacturing practices and normal quality control procedures are used.

(ii) Allow for all sources of variability likely to be encountered in the production process.

(iii) Take into account the stability of the ingredient in the product and the possible formation of impurities between production and sale or distribution.

(4) The applicant may include an explanation of the basis of his proposed certified limits, including how the certified limits were arrived at (*e.g.*, sample analysis, quantitative estimate based on production process), and its accuracy and precision. This will be particularly useful if the range of the certified limit for an active or inert ingredient is greater than the standard certified limits.

(d) *Special cases.* If the Agency finds unacceptable any certified limit (either standard, or applicant proposed), the Agency will inform the registrant or applicant of its determination and will provide supporting reasons. The Agency may also recommend alternative limits to the applicant. The Agency may require, on a case-by-case basis, any or all of the following:

(1) More precise limits.

(2) More thorough explanation of how the certified limits were determined.

(3) A narrower range between the upper and lower certified limits than that proposed.

(e) *Certification statement.* The applicant must certify the accuracy of the information presented, and that the certified limits of the ingredients will be maintained. The following statement, signed by the authorized representative of the company, is acceptable:

I hereby certify that, for purposes of FIFRA sec. 12(a)(1)(C), the description of the composition of [*insert product name*], EPA Reg. No. [*insert registration number*], refers to the composition set forth on the Statement of Formula and supporting materials. This description includes the representations that: (1) No ingredient will be present in the product in an amount greater than the upper certified limit or in an amount less than the lower certified limit (if required) specified for that ingredient in a currently approved Statement of Formula (or as calculated by the Agency); and (2) If the Agency requires that the source of supply of an ingredient be specified, that all quantities of such ingredient will be obtained from the source specified in the Statement of Formula.

§ 158.355 Enforcement analytical method.

An analytical method suitable for enforcement purposes must be provided for each active ingredient in the product and for each other ingredient or impurity that the Agency determines to be toxicologically significant.

g. By adding subpart E to read as follows:

Subpart E—Terrestrial and Aquatic Nontarget Organisms

§ 158.400 Terrestrial and aquatic nontarget organisms data requirements table.

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the terrestrial and aquatic nontarget data requirements for a particular pesticide product. Notes that apply to an individual test including specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

(b) *Use patterns.* (1) The terrestrial use pattern includes products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, and terrestrial nonfood crop. The greenhouse use pattern includes products classified under the general use patterns of greenhouse food crop and greenhouse nonfood crop. The indoor use pattern includes products classified under the general use patterns of indoor food, and indoor nonfood use.

(2) Data are also required for the general use patterns of aquatic food crop, aquatic nonfood residential, aquatic nonfood outdoor, forestry and residential outdoor use.

(3) In general, for all outdoor end-use products including turf, the following studies are required: two avian oral LD_{50}, two avian dietary LC_{50}, two avian reproduction studies, two freshwater fish LC_{50}, one freshwater invertebrate EC_{50}, one honeybee acute contact LD_{50}, one freshwater fish early-life stage, one freshwater invertebrate life-cycle, and three estuarine acute LC_{50}/EC_{50} studies - fish, oyster, and mysid. All other outdoor residential uses, *i.e.*, gardens and ornamental will not usually require the freshwater fish early-life stage, the freshwater invertebrate life-cycle, and the acute estuarine tests.

(c) Key: R=Required; CR=Conditionally required; NR=Not required; []=Required or conditionally required for an experimental use permit; TGAI=Technical grade of the active ingredient; TEP=Typical end-use product; PAI=Pure active ingredient; Commas between the test substances (*i.e.*, TGAI, TEP) indicate that data may be required on the TGAI or the TEP depending on the conditions set forth in the test note.

(d) *Table.* The following table shows the data requirements for nontarget terrestrial and aquatic organism. The table notes are shown in paragraph (e) of this section.

TERRESTRIAL AND AQUATIC NONTARGET ORGANISM DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Pattern								Test substance	Test Note No.
		Terrestrial	Aquatic			Forestry	Residential Outdoor	Greenhouse	Indoor		
			Food	Nonfood							
				Outdoor	Residential						
Avian and Mammalian Testing											
850.2100	Avian oral toxicity	[R]	[R]	[R]	R	[R]	[R]	CR	CR	TGAI, TEP	1, 2, 3, 4
850.2200	Avian dietary toxicity	[R]	[R]	[R]	CR	[R]	[R]	NR	NR	TGAI	1, 3, 5, 6
850.2400	Wild mammal toxicity	CR	CR	CR	NR	CR	CR	NR	NR	TGAI	7
850.2300	Avian reproduction	R	R	R	NR	R	R	NR	NR	TGAI	1, 5
850.2500	Simulated or actual field testing	CR	CR	CR	NR	CR	CR	NR	NR	TEP	8, 9
Aquatic Organisms Testing											

TERRESTRIAL AND AQUATIC NONTARGET ORGANISM DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Pattern								Test substance	Test Note No.
		Terrestrial	Aquatic			Forestry	Residential Outdoor	Greenhouse	Indoor		
			Food	Nonfood							
				Outdoor	Residential						
850.1075	Freshwater fish toxicity	[R]	[R]	[R]	R	[R]	R	CR	CR	TGAI, TEP	1, 2, 10, 11
850.1010	Acute toxicity freshwater invertebrates	[R]	[R]	[R]	R	[R]	R	CR	CR	TGAI, TEP	1, 2, 11, 12
850.1025 850.1035 850.1045 850.1055 850.1075	Acute toxicity estuarine and marine organisms	R	R	R	NR	R	R	NR	NR	TGAI, TEP	1, 11, 13, 14
850.1300	Aquatic invertebrate life-cycle (freshwater)	R	[R]	[R]	NR	[R]	CR	NR	NR	TGAI	1, 12, 14
850.1350	Aquatic invertebrate life-cycle (saltwater)	CR	CR	CR	NR	CR	CR	NR	NR	TGAI	14, 16, 17
850.1400	Fish early-life stage (freshwater)	R	[R]	[R]	NR	[R]	CR	NR	NR	TGAI	1, 14, 15
850.1400	Fish early-life stage (saltwater)	CR	CR	CR	NR	CR	CR	NR	NR	TGAI	14, 17, 18
850.1500	Fish life-cycle	CR	CR	CR	NR	CR	CR	NR	NR	TGAI	19, 20
850.1710 850.1730 850.1850	Aquatic organisms bioavailability, biomagnification, toxicity	CR	CR	CR	NR	CR	NR	NR	NR	TGAI, PAI, degradate	21
850.1950	Simulated or actual field testing for aquatic organisms	CR	CR	CR	NR	CR	CR	NR	NR	TEP	9, 22
Sediment Testing											
850.1735	Whole sediment: acute freshwater invertebrates	CR	CR	CR	NR	CR	NR	NR	NR	TGAI	23
850.1740	Whole sediment: acute marine invertebrates	CR	CR	CR	NR	CR	NR	NR	NR	TGAI	23
--	Whole sediment: chronic invertebrates freshwater and marine	CR	CR	CR	NR	CR	NR	NR	NR	TGAI	24
Insect Pollinator Testing											
850.3020	Honey bee acute contact toxicity	[R]	[R]	[R]	NR	[R]	R	NR	NR	TGAI	1
850.3030	Honey bee toxicity of residues on foliage	CR	CR	CR	NR	CR	CR	NR	NR	TEP	25
850.3040	Field testing for pollinators	CR	CR	CR	CR	CR	CR	NR	NR	TEP	26

TERRESTRIAL AND AQUATIC NONTARGET ORGANISM DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Pattern								Test substance	Test Note No.
		Terrestrial	Aquatic			Forestry	Residential Outdoor	Greenhouse	Indoor		
			Food	Nonfood							
				Outdoor	Residential						
Nontarget Insect Testing											
142–1	Acute toxicity to aquatic insects	--	--	--	--	--	--	--	--	TGAI	27
142–1	Aquatic insect life-cycle	--	--	--	--	--	--	--	--	TEP	27
142–3	Simulated or actual field testing for aquatic insects	--	--	--	--	--	--	--	--	TEP	27
143–1 143–2 143–3	Predators and parasites	--	--	--	--	--	--	--	--	TEP	27

(e) *Test notes*. The following test notes apply to terrestrial and aquatic nontarget organisms data requirements in the table to paragraph (d) of this section:

1. Data using the TGAI are required to support all outdoor end-use product uses including, but not limited to turf. Data are generally not required to support end-use products in the form of a gas, a highly volatile liquid, a highly reactive solid, or a highly corrosive material.

2. For greenhouse and indoor end-use products, data using the TGAI are required to support manufacturing-use products to be reformulated into these same end-use products or to support end-use products when there is no registered manufacturing-use product. Avian acute oral not required for liquid formulations for greenhouse and indoor uses. Study not required if there is no potential for environmental exposure.

3. Data using the TEP are conditionally required based on the results of the avian acute oral (TGAI) and avian subacute dietary tests, intended use pattern, and environmental fate characteristics that indicate potential exposure.

4. Data are preferred on redwing blackbird (*Agelaius phoneiceus*) and either mallard or bobwhite quail for terrestrial, aquatic, forestry, and residential outdoor uses. Data are preferred on mallard or bobwhite quail for indoor and greenhouse uses.

5. Data are preferred on mallard and bobwhite quail.

6. For aquatic nonfood residential uses, data are required to support liquid and solid formulated products on one species if the avian oral LD_{50} of the TGAI is less than or equal to 100 mg a.i./kg. Data on a second species are required if the avian dietary LC_{50} in the first species tested is less than or equal to 500 ppm a.i. in the diet.

7. Tests are required based on the results of lower tier toxicology studies, such as the acute and subacute testing, intended use pattern, and environmental fate characteristics that indicate potential exposure.

8. Tests are required based on the results of lower tier studies such as acute, subacute or reproduction bird and mammal testing, intended use pattern, and environmental fate characteristics that indicate potential exposure.

9. Environmental chemistry methods used to generate data associated with this study must include results of a successful confirmatory method trial by an independent laboratory. Test standards and procedures for independent laboratory validation are available as addenda to the guideline for this test requirement.

10. Data are preferred on rainbow trout and bluegill for terrestrial, aquatic, forestry, and residential outdoor uses. For indoor and greenhouse uses, testing with only one of either fish species is required. Generally, a second species will not be required for indoor and greenhouse use if the selected species LC_{50} is 1 ppm or less. However, if the TGAI is stable in the hydrolysis study, and the LC_{50} value of the first fish tested is between 1 ppm and 10 ppm, then testing with both species is required.

11. Freshwater fish LC_{50} (the most sensitive of the species tested) using the TGAI, freshwater invertebrate EC_{50} (preferably *Daphnia*), and acute LC_{50}/EC_{50} estuarine and marine organisms studies using the EP or TEP are required for any product which meets any of the following conditions:

i. The end-use pesticide will be introduced directly into an aquatic environment (*e.g.*, aquatic herbicides and mosquito larvicides) when used as directed.

ii. The maximum expected environmental concentration (MEEC) or the estimated environmental concentration in the aquatic environment is equal to or greater than one-half the LC_{50} or EC_{50} of the TGAI when the EP is used as directed.

iii. An ingredient in the end-use formulation other than the active ingredient is expected to enhance the toxicity of the active ingredient or to cause toxicity to aquatic organisms.

12. Data are preferred on *Daphnia magna*.

13. Data are preferred on eastern oyster (*Crassostrea virginica*) and oppossum shrimp (*America mysis*) formerly (*Mysidopsis bahia*) and silver side (*Menidia sp.*)

14. Data are generally not required for other, non-turf, outdoor residential uses, *i.e.*, gardens and ornamentals.

15. Data are preferred on rainbow trout. If fathead minnow (*Pimephales promelus*) is used, a 96 hour LC_{50} on that species must also be provided.

16. Data are preferred on oppossum shrimp (*America mysis*) formerly (*Mysidopsis bahia*).

17. Data are required on estuarine species if the product is:

i. Intended for direct application to the estuarine or marine environment.

ii. Expected to enter this environment in significant concentrations because of its expected use or mobility patterns.

iii. If the acute LC_{50} or EC_{50}< 1 mg/l.

iv. If the estimated environmental concentration in water is equal to or greater than 0.01 of the acute EC_{50} or LC_{50} and any of the following conditions exist:

A. Studies of other organisms indicate the reproductive physiology of fish and/or invertebrates may be affected.

B. Physicochemical properties indicate bioaccumulation of the pesticide.

C. The pesticide is persistent in water (*e.g.*, half-life in water greater than 4 days).

18. Data are preferred on sheepshead minnow (*Cypinodon variegatus*).

19. Data are required on estuarine species if the product is intended for direct application to the estuarine or marine environment, or the product is expected to enter this environment in significant concentrations because of its expected use or mobility patterns.

20. Data are required if the end-use product is intended to be applied directly to water, or is expected to be transported to water from the intended use site, and when any of the following conditions apply:

i. If the estimated environmental concentration [See Hazard Evaluation Division Standard Evaluation Procedure Ecological Risk Assessment (EPA–540/09–86–167)] is greater than or equal to 0.1 of the no-observed-effect level in the fish early life-stage or invertebrate life-cycle test;

ii. If studies of other organisms indicate that the reproductive physiology of fish may be affected.

21. Required based on the results of fish or aquatic nontarget organism accumulation studies (guidelines 850.1730 and 850.1950).

22. Tests are required based on the results of lower tier studies such as acute and chronic aquatic organism testing, intended use pattern, and environmental fate characteristics that indicate significant potential exposure.

23. Testing is required if the soil partition coefficient (K_d) is equal to or greater than 50 and the half-life of the pesticide in the sediment is equal to or less than 10 days in either the aerobic soil or aquatic metabolism studies. Registrants should consult with the Agency on appropriate test protocols.

24. Testing is required if:

i. The estimated environmental concentration is equal to or greater than the acute sediment EC_{50}/LC_{50}.

ii. The soil partition coefficient (K_d) is equal to or greater than 50.

(iii) The half-life of the pesticide in the sediment is greater than 10 days in either the aerobic soil or aquatic metabolism studies. Registrants should consult with the Agency on appropriate test protocols.

25. Data required only when the formulation contains one or more active ingredients having an acute LD_{50} of <11 µg/bee as determined in the honey bee acute contact study (guideline 850.3020) and the use pattern(s) indicate(s) that honey bees may be exposed to the pesticide.

26. Required if any of the following conditions are met:

i. Data from other sources (Experimental Use Permit program, university research, registrant submittals, etc.) indicate potential adverse effects on colonies, especially effects other than acute mortality (reproductive, behavioral, etc.);

ii. Data from residual toxicity studies indicate extended residual toxicity.

iii. Data derived from studies with arthropods other than bees that indicate potential chronic, reproductive, or behavioral effects.

27. This requirement is reserved pending further evaluation by EPA to determine what and when data should be required, and to develop appropriate test methods.

h. By adding subpart F to read as follows:

Subpart F—Toxicology

§ 158.500 Toxicology data requirements table.

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the toxicology data requirements for a particular pesticide product. Notes that apply to an individual test and include specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

(b) *Use patterns.* (1) Food use patterns include products classified under the general use patterns of terrestrial food crop use, terrestrial feed crop use, aquatic food crop use, greenhouse food crop use, and indoor food use.

(2) Nonfood use patterns include products classified under the general use patterns of terrestrial nonfood crop use, aquatic nonfood crop use, aquatic nonfood outdoor use, greenhouse nonfood crop use, forestry use, residential outdoor use, indoor nonfood use, and indoor residential use.

(c) *Key.* R=Required; CR=Conditionally required; NR=Not required; []=Required or conditionally required for an experimental use permit; MP=Manufacturing-use product; EP=End-use product; TGAI=Technical grade of the active ingredient; PAI=Pure active ingredient; PAIRA=Pure active ingredient radio-labeled; Choice=Choice of several test substances depending on study required.

(d) *Table.*The following table shows the toxicology data requirements. The table notes are shown in paragraph (e) of this section.

TABLE—TOXICOLOGY DATA REQUIREMENTS

Guideline Number	Data Requirements	Use Pattern		Test substance to support		Test Note No.
		Food	Nonfood	MP	EP	
Acute Testing						
870.1100	Acute oral toxicity—rat	[R]	[R]	MP and TGAI	TGAI, EP, and possibly diluted EP	1, 2
870.1200	Acute dermal toxicity	[R]	[R]	MP and TGAI	TGAI, EP, and possibly diluted EP	1, 2, 3
870.1300	Acute inhalation toxicity - rat	[R]	[R]	MP and TGAI	TGAI and EP	4
870.2400	Primary eye irritation - rabbit	[R]	[R]	MP	TGAI and EP	3
870.2500	Primary dermal irritation	[R]	[R]	MP	TGAI and EP	1, 3
870.2600	Dermal sensitization	[R]	[R]	MP	TGAI and EP	3, 5
870.6100	Delayed neurotoxicity (acute) - hen	[CR]	[CR]	TGAI	TGAI	6
870.6200	Acute neurotoxicity - rat	R	R	TGAI	TGAI	7
Subchronic Testing						
870.3100	90–day Oral - rodent	[R]	CR	TGAI	TGAI	8, 9

TABLE—TOXICOLOGY DATA REQUIREMENTS—Continued

Guideline Number	Data Requirements	Use Pattern		Test substance to support		Test Note No.
		Food	Nonfood	MP	EP	
870.3150	90–day Oral - non-rodent	[R]	CR	TGAI	TGAI	8
870.3200	21/28–day Dermal	R	NR	TGAI	TGAI and EP	10, 11
870.3250	90–day Dermal	CR	R	TGAI	TGAI and EP	11, 12
870.3465	90–day Inhalation - rat	CR	CR	TGAI	TGAI	13, 14
870.6100	28–day Delayed neurotoxicity-hen	CR	CR	TGAI	TGAI	15
870.6200	90–day Neurotoxicity - rat	R	R	TGAI	TGAI	7, 16
Chronic Testing						
870.4100	Chronic oral - rodent and non-rodent	[R]	CR	TGAI	TGAI	17, 18, 19
870.4200	Carcinogenicity - two rodent species - rat and mouse preferred	R	CR	TGAI	TGAI	9, 17, 18, 19, 20, 21
Developmental Toxicity and Reproduction						
870.3700	Prenatal Developmental toxicity - rat and rabbit, preferred	[R]	R	TGAI	TGAI	22, 23, 24, 25, 26
870.3800	Reproduction	[R]	R	TGAI	TGAI	26, 27, 28
870.6300	Developmental neurotoxicity	CR	CR	TGAI	TGAI	26, 27, 28
Mutagenicity Testing						
870.5100 870.5300 870.5375	Bacterial reverse mutation assay *In vitro* mammalian cell assay	[R] [R]	R R	TGAI TGAI	TGAI TGAI	29 29, 30
870.5385 870.5395	*In vivo* cytogenetics	[R]	R	TGAI	TGAI	29, 31
Special Testing						
870.7485	Metabolism and pharmacokinetics	R	CR	PAI or PAIRA	PAI or PAIRA	32
870.7200	Companion animal safety	CR	CR	--	Choice	33
870.7600	Dermal penetration	CR	CR	Choice	Choice	34
870.6500	Scheduled controlled operant behavior	CR	CR	TGAI	TGAI	35
870.6850	Peripheral nerve function	CR	CR	TGAI	TGAI	35
870.6855	Neurophysiology: sensory evoked potentials	CR	CR	TGAI	TGAI	35
870.7800	Immunotoxicity	R	R	TGAI	TGAI	

(e) *Test notes.* The following test notes are applicable to toxicological data requirements in paragraph (d) of this section:

1. Not required if test material is a gas or a highly volatile liquid.

2. Diluted EP testing is required to support the end product registration if results using the EP meet the criteria for restricted use classification under § 152.170(b) or special review consideration under § 154.7(a)(1).

3. Not required if test material is corrosive to skin or has a pH of less than 2 or greater than 11.5.

4. Required if the product consists of, or under conditions of use will result in, a respirable material (*e.g.*, gas, vapor, aerosol, or particulate).

5. Required if repeated dermal exposure is likely to occur under conditions of use.

6. Required if the test material is an organophosphorus substance, which includes uncharged organophosphorus esters, thioesters, or anhydrides of organophosphoric, organophosphonic, or organophosphoramidic acids, or of related phosphorothioic, phosponothioic, or phosphorothioamidic acids, or is structurally related to other substances that may cause the delayed neurotoxicity sometimes seen in this class of chemicals.

7. Additional measurements such as cholinesterase activity for certain pesticides, *e.g.*, organophosphates and some carbamates, will also be required. The route of exposure must correspond with the primary route of exposure.

8. Required in rat for nonfood use pesticides if oral exposure could occur, such as through drinking water.

9. A 90–day range-finding study in both rats and mice is required to determine dose levels if carcinogenicity studies are required. If the mouse carcinogenicity study is not required, the 90–day mouse subchronic study is likewise not required.

10. Required for agricultural uses or if repeated human dermal exposure may occur. Not required if an acceptable 90–day dermal toxicity study is performed and submitted.

11. EP testing is required if the product, or any component of it, may increase dermal absorption of the active ingredient(s) as determined by testing using the TGAI, or increase toxic or pharmacologic effects.

12. Required for food uses if either of the following criteria is met:

i. The use pattern is such that the dermal route would be the primary route of exposure.

ii. The active ingredient is known or expected to be metabolized differently by the dermal route of exposure than by the oral route, and a metabolite is the toxic moiety.

13. Required if there is the likelihood of significant repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol.

14. Based on estimates of the magnitude and duration of human exposure, studies of shorter duration, *e.g.*, 21– or 28–days, may be sufficient to satisfy this requirement. Registrants should consult with the Agency to determine whether studies of shorter duration would meet this requirement.

15. Required if results of acute neurotoxicity study (guideline 870.6100) indicate significant statistical or biological effects, or if other available data indicate the potential for this type of delayed neurotoxicity, as determined by the Agency.

16. All 90–day subchronic studies in rats can be designed to simultaneously fulfill the requirements of the 90–day neurotoxicity study using separate groups of animals for testing. Although the subchronic guidelines include the measurement of neurological endpoints, they do not meet the requirement of the 90–day neurotoxicity study (guideline 870.6200).

17. Required if either of the following are met:

i. The use of the pesticide is likely to result in repeated human exposure over a considerable portion of the human lifespan, as determined by the Agency.

ii. The use requires a tolerance or an exemption from the requirement of a tolerance be established.

18. Based on the results of the acute and subchronic neurotoxicity studies, or other available data, a combined chronic toxicity and neurotoxicity study may be required.

19. Studies which are designed to simultaneously fulfill the requirements of both the chronic oral and carcinogenicity studies (*i.e.*, a combined study under guideline 870.4300) may be conducted. Minimum acceptable study durations are:

i. Chronic rodent feeding study (food use) - 24 months.

ii. Chronic rodent feeding study (nonfood use) - 12 months.

iii. Chronic nonrodent feeding study - 12 months.

iv. Mouse carcinogenicity study - 18 months.

v. Rat carcinogenicity study - 24 months.

20. Required if any of the following, as determined by the Agency, are met:

i. The use of the pesticide is likely to result in significant human exposure over a considerable portion of the human life span which is significant in terms of either time, duration, or magnitude of exposure.

ii. The use requires a tolerance or an exemption from the requirement of a tolerance be established.

iii. The active ingredient, metabolite, degradate, or impurity (A) is structurally related to a recognized carcinogen, (B) causes mutagenic effects as demonstrated by *in vitro* or *in vivo* testing, or (C) produces a morphologic effect in any organ (*e.g.*, hyperplasia, metaplasia) in subchronic studies that may lead to a neoplastic change.

21. If this study is modified or waived, a subchronic 90–day oral study (guideline 870.3100) conducted in the same species may be required.

22. Testing in two species is required for all uses.

23. Unless the chemical or physical properties of the test substance, or the pattern of exposure, suggest a more appropriate route of exposure, the oral route, by oral intubation, is preferred.

24. Additional testing by other routes may be required if the pesticide is determined to be a prenatal developmental toxicant after oral dosing.

25. May be combined with the two-generation reproduction study in rodents (870.3800) by utilizing a second mating of the parental animals in either generation. The dams are to undergo a cesarean section at one day prior to expected delivery date and evaluated separately as specified in guideline 870.3700.

26. An information-based approach to testing is preferred, which utilizes the best available knowledge on the chemical (hazard, pharmacokinetic, or mechanistic data) to determine whether a standard guideline study, an enhanced guideline study, or an alternative study should be conducted to assess potential hazard to the developing animal, or in some cases to support a waiver for such testing. Registrants should submit any alternative proposed testing protocols and supporting scientific rationale to the Agency prior to study initiation.

27. A DNT would be required using a weight-of-the-evidence approach when:

i. The pesticide causes treatment-related neurological effects in adult animal studies (i.e, clinical signs of neurotoxicity, neuropathology, functional or behavioral effects).

ii. The pesticide causes treatment-related neurological effects in developing animals, following pre- and/or postnatal exposure (*i.e.*, nervous system malformations or neuropathy, brain weight changes in offspring, functional or behavioral changes in the offspring).

iii. The pesticide elicits a causative association between exposures and adverse neurological effects in human epidemiological studies.

iv. The pesticide evokes a mechanism that is associated with adverse effects on the development of the nervous system (*i.e.*, SAR relationship to known neurotoxicants, altered neuroreceptor or neurotransmitter responses).

28. The use of a combined study that utilizes the two-generation reproduction study in rodents (870.3800) as a basic protocol for the addition of other endpoints or functional assessments in the immature animal is encouraged.

29. At a minimum, an initial battery of mutagenicity tests with possible confirmatory testing is required. Other relevant mutagenicity tests that may have been performed, plus a complete reference list must also be submitted.

30. Choice of assay using either:

i. Mouse lymphoma L5178Y cells, thymidine kinase (tk) gene locus, maximizing assay conditions for small colony expression or detection.

ii. Chinese hamster ovary (CHO) or Chinese hamster lung fibroblast (V79) cells, hypoxanthine-guanine phosphoribosyl transferase (hgprt) gene locus, accompanied by an appropriate *in vitro* test for clastogenicity.

ii.) CHO cells strains AS52, xanthine-guanine phosphoribosyl transferase (xprt) gene locus.

31. Choice of assays. Assays using rodent bone marrow, using either metaphase analysis (aberrations), or micronucleus assay are preferred.

32. Required when chronic or carcinogenicity studies are required. May be required if significant adverse effects are seen in available toxicology studies and these effects can be further elucidated by metabolism studies.

33. May be required if the product's use will result in exposure to domestic animals through, but not limited to, direct application or consumption of treated feed.

34. Required if toxic effects are identified in the oral or inhalation study. A risk assessment assuming that dermal absorption is equal to oral absorption must be performed to determine if the study is required, and to identify the doses and duration of exposure for which dermal absorption is to be quantified.

35. May be required based on adverse effects seen in the acute or subchronic neurotoxicity screening studies, or other studies, or if the test substance is structurally related to a chemical known to cause effects best assessed by these studies.

§ 158.510 Tiered testing options for nonfood pesticides.

For nonfood use pesticides only, applicants have two options for generating and submitting required toxicology (§ 158.500) and human exposure (§ 158.820, § 158.1110, and § 158.1420) studies. The options in this paragraph do not apply to pesticides used in or on food. Applicants are to select one of the following:

(a) Acute, subchronic, chronic, and other toxicological studies on the active ingredient must be submitted together. The specific makeup of the set of toxicology study requirements is based

on the anticipated exposure to the pesticide as determined by the Agency. If hazards are identified based upon review of these studies, specific exposure data will be required to evaluate risk.

(b) Certain toxicological and exposure studies must be submitted simultaneously with the toxicology data submitted in a tiered system. Exposure data must be submitted along with first tier toxicology data. The requirement for additional second and third level toxicology testing will be determined by the Agency based on the results of the first tiered studies.

(1) The required first-tier toxicology studies consist of:

(i) Battery of acute studies (guidelines 870.1100 - 870.2600)

(ii) A subchronic 90–day dermal study (guideline 870.3250) or a subchronic 90–day inhalation study (guideline 870.3465)

(iii) An acute and subchronic neurotoxicity screening battery in the rat (guidelines 870.6100 and 870.6200); a developmental neurotoxicity study in the rat (guideline 870.6300)

(iv) Prenatal developmental toxicity studies in both the rat and rabbit (guideline 870.3700).

(v) Reproduction and fertility studies in rats (guideline 870.3800)

(vi) Battery of mutagenicity studies (guideline 870.5100 - 870.5395)

(vii) Immunotoxicity study (guideline 870.7800)

(2) The conditionally required second-tier studies include:

(i) Subchronic 90–day feeding studies in both the rodent and nonrodent (guidelines 870.3100 and 870.3150)

(ii) Dermal penetration study (guideline 870.7600)

(3) The conditionally required third-tier studies include:

(i) Chronic feeding studies in both the rodent and nonrodent (guideline 870.4100)

(ii) Carcinogenicity (guidelines 870.4200)

(iii) Metabolism study (guideline 870.7485)

(iv) Additional mutagenicity testing (no guideline number)

Subpart G—Product Performance

i. By adding subpart G entitled ''Product Performance''.

§ 158.610 [Redesignated from § 158.640]

j. By redesignating § 158.640 as § 158.610 and adding redesignated § 158.610 to subpart G.

Subparts H-I [Reserved]

k. By adding and reserving subparts H and I.

l. By adding subpart J to read as follows:

Subpart J—Nontarget Plant Protection

§ 158.700 Nontarget plant protection data requirements Table.

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the nontarget plant data requirements for a particular pesticide product. Notes that apply to an individual test include specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

(b) *Use patterns.* (1) The terrestrial use pattern includes products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, and terrestrial nonfood. The aquatic use pattern includes the general use patterns of aquatic food crop, aquatic nonfood residential, and aquatic nonfood outdoors.

(2) Data are also required for the general use patterns of forestry use and residential outdoor use.

(c) *Key.* R=Required; CR=Conditionally required; NR=Not required; TGAI=Technical grade of the active ingredient; TEP=Typical end-use product.

(d) *Table.* The following table shows the nontarget plant protection data requirements. The table notes are shown in paragraph (e) of this section.

TABLE—NONTARGET PLANT PROTECTION DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Pattern			Test substance	Test Note No.
		Terrestrial	Aquatic	Forestry and Residential Outdoor		
Nontarget Area Phytotoxicity - Tier I						
850.4100	Seedling emergence	R	R	R	TEP	1, 2, 3
850.4150	Vegetative vigor	R	R	R	TEP	1, 2
850.4400 850.5400	Aquatic plant growth (algal and aquatic vascular plant toxicity)	R	R	R	TEP or TGAI	1, 2
Nontarget Area Phytotoxicity - Tier II						
850.4225	Seedling emergence	CR	CR	CR	TEP	1, 3, 4, 5
850.4250	Vegetative vigor	CR	CR	CR	TEP	1, 4, 5
850.4400 850.5400	Aquatic plant growth (algal and aquatic vascular plant toxicity)	CR	CR	CR	TEP or TGAI	1, 4, 6
Nontarget Area Phytotoxicity - Tier III						
850.4300	Terrestrial field	CR	CR	CR	TEP	1, 7, 8
850.4450	Aquatic field	CR	CR	CR	TEP	1, 8
Target Area Phytotoxicity						
850.4025	Target area phytotoxicity	CR	CR	CR	TEP	1, 7, 9

(e) *Test notes.* The following test notes apply to the table in paragraph (d) of this section.

1. Not required for contained pesticide treatments such as bait boxes and pheromone traps unless adverse effects reports are received by the Agency.
2. Required for all outdoor pesticide uses except for known phytotoxicants (such as herbicides, desiccants, defoliants).
3. Generally not required for granular formulations. May be requested on a case-by-case basis.
4. Required for known phytotoxicants such as herbicides, desiccants, defoliants, and plant growth regulators.
5. Required if a terrestrial species exhibits a 25 percent or greater detrimental effect in Tier I.
6. Required if an aquatic species exhibits a 50 percent or greater detrimental effect in Tier I.
7. Not required for aquatic residential uses.
8. Environmental chemistry methods used to generate data must include results of a successful confirmatory method trial by an independent laboratory.
9. Tests are required based on the results of lower tier phytotoxicity studies, adverse incident reports, intended use pattern, and environmental fate characteristics that indicate potential exposure.

m. By adding subpart K to read as follows:

Subpart K—Post-application Exposure

§ 158.800 General requirements.

(a) Certain measures taken to reduce or mitigate exposure may affect the need for data. Where label, formulation, or packaging and use restrictions, *e.g.*, child-resistant bait stations, are expected to significantly decrease or eliminate exposure, these data requirements may not be required.

(b) If EPA determines that industrial standards, such as the workplace standards set by Occupational Safety and Health Administration, provide adequate protection for a particular pesticide use pattern, post-application exposure data may not be required for that use pattern. Applicants should consult with the Agency on appropriate testing before the initiation of studies.

(c) The Agency may accept surrogate exposure data from other sources to satisfy post-application exposure data requirements if the data meet the basic quality assurance, quality control, good laboratory practice, and other scientific needs of EPA. In order to be acceptable, among other things, the Agency must find that the surrogate exposure data have adequate information to address post-application exposure data requirements and contain adequate replicates of acceptable quality data to reflect the specific use prescribed on the label and the post-application activity of concern, including formulation type, application methods and rates, type of activity, and other pertinent information. The Agency will consider using such surrogate data for evaluating human exposure on a case-by-case basis.

§ 158.810 Criteria for testing

Exposure data described in § 158.820(d) are required based upon toxicity and exposure criteria. Data are required if a product meets, as determined by the Agency, either or both of the toxicity criteria in paragraph (a) of this section and either or both of the exposure criteria in paragraph (b) of this section.

(a) *Toxicity criteria.* (1) Evidence of potentially significant adverse health effects have been observed in any applicable toxicity studies.

(2) Scientifically sound epidemiological or poisoning incident data indicate that adverse health effects may have resulted from post-application exposure to the pesticide.

(b) *Exposure criteria.* When there is potential exposure to humans from post-application pesticide residues from any media, typically, these exposures fall into the following areas.

(1) *For outdoor uses.* (i) Occupational human post-application exposure to pesticide residues on plants or in soil could occur as the result of cultivation, pruning, harvesting, mowing or other work related activity. Such plants include agricultural food, feed, and fiber commodities, forest trees, ornamental plants, and turf grass.

(ii) Residential human post-application exposure to pesticide residues on plants or in soil could occur. Such plants may include turf grass, fruits, vegetables, and ornamentals grown at sites, including, but not limited to, homes, parks, and recreation areas.

(2) *For indoor uses.* (i) Occupational human post-application exposure to pesticide residues could occur following the application of the pesticide to indoor spaces or surfaces at agricultural or commercial sites, such as, but not limited to, agricultural animal facilities and industrial or manufacturing facilities.

(ii) Residential human post-application exposure to pesticide residues could occur following the application of the pesticide to indoor spaces or surfaces at residential sites, such as, but not limited to, inside homes, daycare centers, hospitals, schools, and other public buildings.

The need for data from potential exposure resulting from situations not covered by these examples should be discussed with the Agency.

§ 158.820 Post-application exposure data requirements table

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the post-application data requirements for a particular pesticide product. Notes that apply to an individual test and include specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

(b) *Use patterns.* (1) Occupational use patterns include products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, terrestrial nonfood use, aquatic food crop, aquatic nonfood use, aquatic nonfood outdoor, aquatic nonfood industrial, forestry, greenhouse food, greenhouse nonfood, indoor food, and indoor nonfood. Occupational use patterns also include commercial (''for hire'') applications to residential outdoor and indoor sites.

(2) Residential use patterns include residential outdoor use and indoor residential use. These use patterns are limited to nonoccupational,*i.e.*, nonprofessional, pesticide applications.

(c) *Key.* R=Required; CR=Conditionally required; NR=Not required; TEP=Typical End-use product.

(d) *Table.* The data requirements listed in the following table pertain to pesticide products that meet the testing criteria outlined in § 158.810. The table notes are shown in paragraph (e) of this section.

POST-APPLICATION EXPOSURE DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Pattern		Test Substance	Test Note No.
		Occupational	Residential		
875.2100	Dislodgeable foliar residue and turf transferable residues	R	R	TEP	1, 2, 3, 4, 5

POST-APPLICATION EXPOSURE DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Pattern		Test Substance	Test Note No.
		Occupational	Residential		
875.2200	Soil residue dissipation	R	CR	TEP	1, 2, 6, 7
875.2300	Indoor surface residue dissipation	R	R	TEP	1, 2, 8, 9
875.2400	Dermal exposure	R	R	TEP	1, 2, 10, 11, 12
875.2500	Inhalation exposure	R	R	TEP	1, 10, 11, 12
875.2600	Biological monitoring	CR	CR	TEP	1, 12, 13
875.2700	Product use information	R	R	TEP	--
875.2800	Description of human activity	R	R	TEP	--
875.2900	Data reporting and calculations	R	R	TEP	14
875.3000	Nondietary ingestion exposure	NR	R	TEP	1, 11, 15

(e) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (d) of this section:

1. Protocols must be submitted for approval prior to the initiation of the study. Details for developing protocols are available from the Agency.

2. Bridging applicable residue dissipation data to dermal exposure data is required.

3. Turf grass transferable residue dissipation data are required when pesticides are applied to turf grass. Dislodgeable foliar residue dissipation data are required when pesticides are applied to the foliage of plants other than turf grass.

4. Data are required for occupational sites, if (i) there are uses on turf grass or other plant foliage, and (ii) the human activity data indicate that workers are likely to have post-application dermal contact with treated foliage while participating in typical activities.

5. Data are required for residential sites if there are uses on turf grass or other plant foliage.

6. Data are required for occupational sites, if (i) there are outdoor or greenhouse uses to or around soil or other planting media, and (ii) the human activity data indicate that workers are likely to have post-application dermal contact with treated soil or planting media while participating in typical activities.

7. Data are required for residential sites if the pesticide is applied to or around soil or other planting media both outdoors and indoors, *e.g.*, residential greenhouse or houseplant uses.

8. Data are required for occupational sites if the pesticide is applied to or around on non-plant surfaces, *e.g.*, flooring or countertops, and if the human activity data indicate that workers are likely to have post-application dermal contact with treated indoor surfaces while participating in typical activities.

9. Data are required for residential sites if the pesticide is applied to or around non-plant surfaces, *e.g.*, flooring and countertops.

10. Data are required for occupational sites if the human activity data indicate that workers are likely to have post-application exposures while participating in typical activities.

11. Data are required for residential sites if post-application exposures are likely.

12. Biological monitoring data may be submitted in addition to, or in lieu of, dermal and inhalation exposure data provided the human pharmocokinetics of the pesticide and/or metabolite/analog compounds (*i.e.*, whichever method is selected as an indicator of body burden or internal dose) allow for a back-calculation to the total internal dose.

13. Data are required when passive dosimetry techniques are not applicable for a particular exposure scenario, such as a swimmer exposure to pesticides.

14. Data reporting and calculations are required when any post-application exposure monitoring data are submitted.

15. The selection of a sampling method will depend on the nondietary pathway(s) of interest. Data must be generated to consider all potential pathways of nondietary ingestion exposure that are applicable (*e.g.*, soil ingestion, hand-to-mouth transfer, and object-to-mouth transfer of surface residues).

Subpart L—Biochemical Pesticides

n. By adding subpart L entitled ''Biochemical Pesticides.''

§ 158.910 [Redesignated from § 158.690]

o. By redesignating § 158.690 as § 158.910 and adding § 158.910 to subpart L.

Subpart M—Microbial Pesticides

p. By adding subpart M entitled ''Microbial Pesticides.''

§ 158.1010 [Redesignated from 158.740]

q. By redesignating § 158.740 as § 158.1010 and adding redesignated § 158.1010 to subpart M.

r. By adding subpart N to read as follows:

Subpart N—Environmental Fate

§ 158.1100 Environmental Fate Data Requirements Table.

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the environmental fate data requirements for a particular pesticide product. Notes that apply to an individual test including specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

(b) *Use patterns.* (1) The terrestrial use pattern includes products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, and terrestrial nonfood. The aquatic use pattern includes the general use patterns of aquatic food crop, aquatic nonfood residential, and aquatic nonfood outdoors. The greenhouse use pattern includes both food and nonfood uses. The indoor use pattern includes food, nonfood, and residential indoor uses.

(2) Data are also required for the general use patterns of forestry use and residential outdoor use.

(c) *Key.* R=Required; CR=Conditionally required; NR=Not required; []=Required or conditionally required for an experimental use permit; TGAI=Technical grade of the active ingredient; TEP=Typical end-use product; PAIRA=Pure active ingredient radio-labeled.

(d) *Table.*The following table list the data requirements that pertain to environmental fate. The table notes are shown in paragraph (e) of this section.

ENVIRONMENTAL FATE DATA REQUIREMENTS

Guideline Number	Data requirement	Use pattern						Test substance	Test Note No.
		Terrestrial	Aquatic	Greenhouse	Indoor	Forestry	Residential Outdoors		
Degradation Studies—Laboratory									
835.2120	Hydrolysis	[R]	[R]	[R]	CR	[R]	[R]	TGAI or PAIRA	1
835.2240	Photodegradation in water	R	R	NR	NR	R	NR	TGAI or PAIRA	2
835.2410	Photodegradation on soil	R	NR	NR	NR	R	NR	TGAI or PAIRA	3
835.2370	Photodegradation in air	CR	NR	CR	NR	CR	CR	TGAI or PAIRA	4
Metabolism Studies - Laboratory									
835.4100	Aerobic soil	[R]	CR	R	NR	[R]	R	TGAI or PAIRA	5
835.4200	Anaerobic soil	R	NR	NR	NR	NR	NR	TGAI or PAIRA	--
835.4300	Aerobic aquatic	R	[R]	NR	NR	R	NR	TGAI or PAIRA	--
835.4400	Anaerobic aquatic	R	R	NR	NR	R	NR	TGAI or PAIRA	--
Mobility Studies									
835.1230 835.1240	Leaching and adsorption/ desorption	[R]	R	R	NR	[R]	R	TGAI or PAIRA	--
835.1410	Volatility - laboratory	CR	NR	CR	NR	NR	NR	TEP	4
835.8100	Volatility - field	CR	NR	CR	NR	NR	NR	TEP	--
Dissipation Studies - Field									
835.6100	Terrestrial	R	CR	NR	NR	NR	R	TEP	5, 6
835.6200	Aquatic (sediment)	CR	R	NR	NR	NR	NR	TEP	6, 7
835.6300	Forestry	NR	NR	NR	NR	CR	NR	TEP	6, 8
835.6400	Combination and tank mixes	CR	CR	NR	NR	NR	NR	TEP	9
Accumulation Studies									
850.1730	Fish	[CR]	[CR]	NR	NR	[CR]	NR	TGAI or PAIRA	10
850.1950	Aquatic nontarget organisms	CR	CR	NR	NR	CR	NR	TEP	11
Ground Water Monitoring									
835.7100	Ground water monitoring	CR	NR	NR	NR	CR	NR	TEP	6, 8, 12

(e) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (d) of this section.

1. Study is required for indoor uses in cases where environmental exposure is likely to occur. Such sites include, but are not limited to, agricultural premises, in or around farm buildings, barnyards, and beehives.

2. Not required when the electronic absorption spectra, measured at pHs 5, 7, and 9, of the chemical and its hydrolytic products, if any, show no absorption or tailing between 290 and 800 nm.

3. Not required when the chemical is to be applied only by soil injection or is incorporated in the soil.

4. Requirement based on use patterns and other pertinent factors including, but not limited to, Henry's Law Constant. In view of methodological difficulties with the study of photodegradation in air, prior consultation with the Agency regarding the protocol is recommended before the test is performed.

5. Required for aquatic food and nonfood crop uses for aquatic sites that are intermittently dry. Such sites include, but are not limited to cranberry bogs and rice paddies.

6. Environmental chemistry methods used to generate data associated with this study must include results of a successful confirmatory method trial by an independent laboratory. The environmental chemistry methods must include a statement of no data confidentiality claims, *i.e.*, non-CBI. Test standards and procedures for independent laboratory validation are available as addenda to the guideline for this test requirement.

7. Requirement for terrestrial uses is based on potential for aquatic exposure and if pesticide residues have the potential for persistence, mobility, nontarget aquatic toxicity or bioaccumulation. Not required for aquatic residential uses.

8. Agency approval of a protocol is necessary prior to initiation of the study.

9. Requirement based on use patterns and other environmental factors that indicate potential exposure.

10. Not required when the octanol/water partition coefficients of the pesticide and its major degradates are less than 1,000; or there are no potential exposures to fish and other nontarget aquatic organisms; or the hydrolytic half-life is less than 5 days at pH 5, 7, and 9.

11. Required if significant concentrations of the active ingredient and/or its principal degradation products are likely to occur in aquatic environments and may accumulate in aquatic organisms.

12. Required if the weight of evidence indicates that the pesticide and/or its degradates is likely to leach to ground water, taking into account other factors such as the toxicity of the chemicals(s), available monitoring data, and the vulnerability of ground water resources in the pesticide use area.

s. Subpart O is added to read as follows:

Subpart O—Residue Chemistry

§ 158.1200 Definitions.

The following terms are defined for the purposes of this subpart:

Livestock, for the purposes of this section, includes all domestic animals that are bred for human consumption, including, but not limited to, cattle, swine, sheep, and poultry.

Plant or animal metabolite means a pesticide chemical residue that is the result of biological breakdown of the parent pesticide within the plant or animal.

Residue of concern means the parent pesticidal compound and its metabolites, degradates, and impurities of toxicological concern.

Tolerance, for the purposes of this section, includes the establishment of a new tolerance or tolerance exemption, or amended tolerance or tolerance exemption.

§ 158.1210 Residue chemistry data requirements table.

(a) *General.* (1) Sections 158.100 through 158.130 describe how to use this table to determine the residue chemistry data requirements for a particular pesticide product. Notes that apply to an individual test and include specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

(2) All residue chemistry data requirements, as described in this section, are required for an experimental use permit.

(b) *Use patterns.* (1) Data are required or conditionally required for all pesticides used in or on food and for residential outdoor uses where food crops are grown. Food use patterns include products classified under the general use patterns of terrestrial food crop use, terrestrial feed crop use, aquatic food crop use, greenhouse food crop use, and indoor food use.

(2) Data may be required for nonfood uses if pesticide residues may occur in food or feed as a result of the use. Data requirements for these nonfood uses will be determined on a case-by-case basis. For example, most products used in or near kitchens require residue data for risk assessment purposes even though tolerances may not be necessary in all cases. Food uses in general require a more extensive database to characterize the extent of the exposure, whereas nonfood uses which are of shorter duration, may require fewer studies. Uses include products classified under the general use patterns of terrestrial nonfood crop use, aquatic nonfood crop use, aquatic nonfood outdoor use, greenhouse nonfood crop use, forestry use, indoor nonfood use, and indoor residential use.

(c) *Key.* R=Required; CR=Conditionally required; NR=Not required; TGAI=Technical grade of the active ingredient; PAI=Pure active ingredient; PAIRA=Pure active ingredient radio-labeled; Residue of concern= the active ingredient and its metabolites, degradates, and impurities of toxicological concern; TEP=Typical end-use product.

(d) *Table.* The following table list the data requirements for residue chemistry related to food uses. The table notes are shown in paragraph (e) of this section.

TABLE—RESIDUE CHEMISTRY DATA REQUIREMENTS FOR FOOD USES

Guideline Number	Data Requirement	Use Pattern					Test substance	Test Note No.
		Terrestrial Food or Feed	Aquatic Food	Greenhouse Food	Indoor Food	Residential Outdoor		
Supporting Information								
860.1100	Chemical identity	R	R	R	R	R	TGAI	--
860.1200	Directions for use	R	R	R	R	R	--	--
860.1550	Proposed tolerance	R	R	R	CR	NR	--	1
860.1560	Reasonable grounds in support of petition	R	R	R	CR	NR	--	1
860.1650	Submittal of analytical reference standards	R	R	R	CR	NR	PAI and residue of concern	1, 2
Nature of the residue								
860.1300	Nature of the residue in plants	R	R	R	CR	CR	PAIRA	3, 4

TABLE—RESIDUE CHEMISTRY DATA REQUIREMENTS FOR FOOD USES—Continued

Guideline Number	Data Requirement	Use Pattern					Test substance	Test Note No.
		Terrestrial Food or Feed	Aquatic Food	Greenhouse Food	Indoor Food	Residential Outdoor		
860.1300	Nature of the residue in livestock	CR	CR	CR	CR	NR	PAIRA or radiolabeled plant metabolite	1, 5, 6
860.1850	Confined rotational crops	CR	CR	NR	NR	NR	PAIRA	7
Analytical methods								
860.1340	Residue analytical methods	R	R	R	CR	CR	Residue of concern	1, 3, 8, 9, 10
860.1360	Multiresidue method	R	R	R	CR	NR	Residue of concern	1, 11
Magnitude of the residue								
860.1380	Storage stability	R	R	R	CR	CR	TEP or residue of concern	1, 3, 10, 12
860.1500	Crop field trials	R	R	R	CR	CR	TEP	3, 10, 14
860.1520	Processed food or feed	CR	CR	CR	CR	NR	TEP	1, 15
860.1480	Meat/milk/poultry/eggs	CR	CR	CR	CR	NR	TGAI or plant metabolite	1, 16, 17, 18
860.1400	Potable water	NR	R	NR	NR	NR	TEP	19
860.1400	Fish	NR	R	NR	NR	NR	TEP	5
860.1400	Irrigated crops	NR	CR	NR	NR	NR	TEP	20
860.1460	Food handling	NR	NR	NR	CR	NR	TEP	1, 21
860.1540	Anticipated residues	CR	CR	CR	CR	NR	Residue of concern	1, 13, 22
860.1900	Field rotational crops	CR	CR	NR	NR	NR	TEP	23

(e) *Test notes.* The following test notes apply to the data requirements in the table to paragraph (d) of this section.

1. Required if indoor use could result in pesticide residues in or on food or feed.

2. Material safety data sheets must accompany standards as specified by OSHA in 29 CFR 1910.1200.

3. Required for residential outdoor use on food crops if home gardens are to be treated or the home garden use is different from the agricultural use pattern on which the tolerance is established.

4. Required for indoor uses where the pesticide is applied directly to food, in order to determine metabolites and/or degradates. Not required when only indirect contact with food would occur (*e.g.*, crack and crevice treatments).

5. Data for fish are required for all pesticides applied directly to water inhabited, or will be inhabited, by fish that may be caught or harvested for human consumption.

6. Required when a pesticide is to be applied directly to livestock, to livestock premises, to livestock drinking water, or to crops used for livestock feed. If results from the plant metabolism study show differing metabolites in plants from those found in animals, an additional livestock metabolism study involving dosing with the plant metabolite(s) may also be required.

7. Required when it is reasonably foreseeable that a food or feed crop could be subsequently planted on the site of the pesticide application.

8. A residue analytical method suitable for enforcement purposes is required whenever a numeric tolerance (including temporary and time-limited tolerance) is proposed, and may be required for a tolerance exemption.

9. New analytical methods to be used for enforcement purposes must include results from an independent laboratory validation.

10. A residue method, storage stability data, and crop field trials are required for the nonfood crop tobacco (green, freshly harvested). Depending on the level of residues found on the green tobacco, additional data may be required on cured/dried tobacco and pyrolysis products (guideline 860.1000).

11. Data are required to determine whether FDA/USDA multiresidue methodology would detect and identify the pesticides and any metabolites.

12. Data are required for any magnitude of the residue study unless analytical samples

are stored frozen for 30 days or less, and the active ingredient is not known to be volatile or labile.

13. Studies using single serving samples of a raw agricultural commodity may be needed for acutely toxic pesticides and/or their metabolites. These residue studies must be conducted using a statistical design accepted by the Agency.

14. Required for indoor uses which are direct postharvest treatments of raw agricultural commodities (*e.g.*, fungicidal waxes or stored grain fumigants).

15. Data on the nature and level of residues in processed food/feed are required if residues could potentially concentrate on processing thus requiring the establishment of a separate tolerance higher than that of the raw agricultural commodity. Studies, however, may be waived if it can be demonstrated that residues do not concentrate on processing.

16. Required when the pesticide use is a direct application to livestock.

17. Data are required if pesticide residues are present in or on livestock feed items. These studies, however, may be waived by the Agency in cases where the residue levels are low or the animal metabolism studies indicate negligible transfer of the pesticide and/or metabolite(s) to tissues, milk, and eggs.

18. If results from the plant metabolism study show differing metabolites in plants from those found in animals, an additional livestock feeding study involving dosing with the plant metabolite(s) may also be required.

19. Data are required whenever a pesticide may be applied directly to water, unless it can be demonstrated that the treated water would not be available for human or livestock consumption.

20. Data are required when a pesticide is to be applied directly to water that could be used for irrigation or to irrigation facilities such as irrigation ditches.

21. Data are required whenever a pesticide may be used in a food handling or feed handling establishment.

22. Required when residues at the tolerance level may result in a risk of concern. These data may include washing, cooking, processing or degradation studies as well as market basket surveys for a more precise residue determination.

23. Required if pesticide or metabolite residues of toxicological concern are found in crops at the appropriate plant back intervals from a confined rotational crop study (guideline 860.1850).

Subpart P—Pesticide Management and Disposal

t. By adding subpart P consisting of § 158.1300 which is reserved.

Subpart R—Spray Drift

u. By adding subpart R entitled ''Spray Drift.''

§ 158.1410 [Redesignated from 158.440]

v. By redesignating § 158.440 as § 158.1410 and adding redesignated § 158.1410 to subpart R.

w. Subpart U is added to read as follows:

Subpart U—Applicator Exposure

§ 158.1500 General requirements.

(a) If EPA determines that industrial standards, such as the workplace standards set by OSHA, provide adequate protection from risk under FIFRA for a particular pesticide use pattern, exposure data may not be required for that use pattern. Applicants should consult with the Agency on appropriate testing prior to the initiation of studies.

(b) The Agency may accept surrogate exposure data estimations from other sources to satisfy applicator exposure data requirements if the data meet the basic quality assurance, quality control, good laboratory practice, and other scientific requirements set by EPA. In order to be acceptable, the Agency must find that the surrogate exposure data estimations have adequate information to address applicator exposure data requirements and contain adequate replicates of acceptable quality data to reflect the specific use prescribed on the label and the applicator activity of concern, including formulation type, application methods and rates, type of activity, and other pertinent information. The Agency will consider using such surrogate data for evaluating human exposure on a case-by-case basis.

§ 158.1510 Criteria for testing.

Applicator exposure data are required based on toxicity and exposure criteria. Data are required if a product meets, as determined by the Agency, at least one of the toxicity criteria in paragraph (a) of this section and either of the exposure criteria in paragraph (b) of this section.

(a) *Toxicity criteria.* (1) Evidence of potentially significant adverse effects have been observed in any applicable toxicity studies.

(2) Scientifically sound epidemiological or poisoning incident data indicate that adverse health effects may have resulted from handling of the pesticide.

(b) *Exposure criteria.* (1) Dermal exposure may occur during the prescribed use.

(2) Respiratory exposure may occur during the prescribed use.

§ 158.1520 Applicator exposure data requirements table.

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the application data monitoring data requirements for a particular pesticide product. Notes that apply to an individual test and include specific conditions, qualifications, or exceptions to the designated test are listed in paragraph (e) of this section.

(b) *Use patterns.* (1) Occupational use patterns include products classified under the general use patterns of terrestrial food crop, terrestrial feed crop, terrestrial nonfood use, aquatic food crop, aquatic nonfood use, aquatic nonfood outdoor, aquatic nonfood industrial, forestry, greenhouse food, greenhouse nonfood, indoor food use, indoor nonfood use, and indoor medical use. Occupational use patterns also include commercial (''for hire'') applications to residential outdoor and indoor sites.

(2) Residential use patterns include residential outdoor use and indoor residential use. These use patterns are limited to nonoccupational,*i.e.*, nonprofessional, pesticide applications.

(c) *Key.* R=Required; CR=Conditionally required; TEP=Typical end-use product.

(d) *Table.* The data requirements listed pertain to pesticide products that meet the testing criteria outlined in § 158.1510. The table notes are shown in paragraph (e) of this section.

APPLICATOR EXPOSURE DATA REQUIREMENTS

Guideline Number	Data requirement	Use pattern		Test substance	Test Note No.
		Occupational	Residential		
875.1100	Dermal outdoor exposure	R	R	TEP	1, 2, 3, 4
875.1200	Dermal indoor exposure	R	R	TEP	1, 2, 5, 6
875.1300	Inhalation outdoor exposure	R	R	TEP	1, 2, 3, 4