

**ENVIRONMENTAL PROTECTION AGENCY****40 CFR Parts 158 and 172**

[EPA-HQ-OPP-2004-0415; FRL-7763-4]

RIN 2070-AD51

**Pesticides; Data Requirements for Biochemical and Microbial Pesticides****AGENCY:** Environmental Protection Agency (EPA).**ACTION:** Proposed rule.

**SUMMARY:** EPA is proposing to update and revise its data requirements for the registration of microbial and biochemical pesticide products to reflect current scientific knowledge. These proposed revisions are intended to provide EPA with data and other information necessary to support the registration of a biochemical and microbial pesticide product, and will improve the Agency's ability to make regulatory decisions about the human health and environmental effects of these pesticide products. EPA is also proposing to update the definitions of a biochemical pesticide and a microbial pesticide to more accurately describe these categories of pesticides, and to make a conforming change to the definition of microbial pesticide. EPA is announcing its policy to provide assistance to applicants when needed in determining what data are appropriate to support registration of a biochemical or microbial pesticide and encouraging applicants to request pre-submission meetings to discuss these data issues. EPA is announcing its intent to provide assistance to applicants in some narrow circumstances in preparation of an applicant's data waiver.

**DATES:** Comments must be received on or before June 6, 2006.**ADDRESSES:** Submit your comments, identified by docket identification (ID) number EPA-HQ-OPP-2004-0415, by one of the following methods:

*Federal eRulemaking Portal:* <http://www.regulations.gov>. Follow the on-line instructions for submitting comments.

*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. In addition, please mail a copy of your comments on the information collection provisions to the Office of Information and Regulatory Affairs, Office of Management and Budget (OMB), Attn: Desk Officer for EPA, 725 17th St. NW., Washington, DC 20503.

*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. EPA-HQ-OPP-2006-0415. 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.regulations.gov/>, 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 [regulations.gov](http://www.regulations.gov) or e-mail. The [regulations.gov](http://www.regulations.gov) website is an "anonymous access" system, 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 [regulations.gov](http://www.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 the EPA Docket Center homepage at <http://www.epa.gov/epahome/dockets.htm>.

*Docket:* All documents in the docket are listed in the [regulations.gov](http://www.regulations.gov) index. Although listed in the index, some information is not publicly available, e.g., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, will be publicly available only in hard copy. Publicly available docket materials are available either electronically in <http://www.regulations.gov> or in hard copy at the Public Information and Records Integrity Branch (PIRIB) (7502C), Office of Pesticide Programs (OPP), Environmental Protection Agency, 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:**

Candace Brassard or Nathanael Martin, U.S. Environmental Protection Agency (7506C), 1200 Pennsylvania Ave. NW., Washington, DC 20460, telephone: 703-305-6598 or 703-305-6475, e-mail: [brassard.candace@epa.gov](mailto:brassard.candace@epa.gov) or [martin.nathanael@epa.gov](mailto:martin.nathanael@epa.gov). Do not e-mail your comments to these contacts. Submit your comments according to the instructions under **ADDRESSES**.

**SUPPLEMENTARY INFORMATION:****I. General Information***A. Does this Action Apply to Me?*

You may be affected by this notice if you are a producer or registrant of a biochemical or microbial pesticide product. This proposal also may affect any person or company who might petition the Agency for new tolerances for biochemical or microbial pesticides, or 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 for biochemical or microbial pesticides. The following is intended as a guide to entities likely to be regulated by this action. The North American Industrial Classification System (NAICS) codes are provided to assist you in determining whether or not this action applies to you. 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.
- Crop Production (NAICS 111).
- Animal Production (NAICS 112).
- Food Manufacturing and Processing (NAICS 311).

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 could also be affected. If you have questions regarding the applicability of this action to a particular entity, please consult the appropriate Branch Chief in the U.S. EPA Biopesticides and Pollution Prevention Division of the Office of Pesticide Programs at 703-308-8712, fax number at 703-308-7026 or visit the following website: <http://www.epa.gov/pesticides/biopesticides/>.

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

1. *Submitting CBI.* Do not submit this information to EPA through [www.regulations.gov](http://www.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:

- i. Identify the document by docket number and other identifying information (subject heading, **Federal Register** date and page number).
- ii. 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.
- iii. Explain why you agree or disagree; suggest alternatives and substitute language for your requested changes.
- iv. Describe any assumptions and provide any technical information and/or data that you used.
- v. If you estimate potential costs or burdens, explain how you arrived at your estimate in sufficient detail to allow for it to be reproduced.
- vi. Provide specific examples to illustrate your concerns, and suggest alternatives.
- vii. Explain your views as clearly as possible, avoiding the use of profanity or personal threats.
- viii. Make sure to submit your comments by the comment period deadline identified.

## II. Overview of EPA's Proposal

EPA is proposing to update and revise its data requirements for the registration of microbial and biochemical pesticide products to reflect current scientific knowledge. These proposed revisions are intended to provide EPA with data and other information necessary to support the registration of a biochemical and microbial pesticide product, and will improve the Agency's ability to make regulatory decisions about the human health and environmental effects of these pesticide products.

Since the data requirements were first codified in 1984, information needed to support the registration of a biochemical and microbial pesticide has evolved as the general scientific understanding of the potential hazards posed by pesticides has grown. Since 1984, EPA has developed new and revised data requirements with public participation, extensive involvement by the scientific community, and review by the Scientific Advisory Panel (SAP) under Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), which have been imposed on a case-by-case basis. By codifying these data requirements, the pesticide industry, along with other partners in the regulated community, will have a better understanding of and could better prepare for the registration process for biochemical and microbial pesticides. In addition, the Agency is proposing certain new data requirements in response to the need for strengthened risk assessment mandated by the Food Quality Protection Act (FQPA) and FIFRA.

EPA is also proposing to update the definitions of a biochemical pesticide and a microbial pesticide to more accurately describe these categories of pesticides, and to make a conforming change to the definition of microbial pesticide in 40 CFR part 172. EPA is announcing its policy to provide assistance to applicants when needed in determining what data are appropriate to support registration of a biochemical or microbial pesticide and encouraging applicants to request pre-submission meetings to discuss these data issues. EPA is announcing its intent to provide assistance to applicants in some narrow circumstances in preparation of an applicant's data waiver.

This proposed rule is one in a series of proposals to update and clarify pesticide data requirements. EPA proposed data requirements for conventional pesticides (70 FR 12276, March 11, 2005) and is developing data requirements specific to antimicrobial pesticides. In the future, EPA expects to develop data requirements for plant-incorporated protectants.

## III. Statutory Authorities and Regulatory Framework

EPA is authorized to regulate pesticides under two Federal statutes. 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 FQPA to strengthen the protections offered, with

particular emphasis on protection of children.

This action is issued under the authority of sections 3, 4, 5, 12, and 25 of FIFRA (7 U.S.C. 136–136y) and section 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

In general, under FIFRA, every pesticide product must be registered (or specifically exempted from registration under FIFRA section 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 determination, as defined in the statute, requires the Agency to consider the risks and benefits associated with the use of a pesticide. 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 fate properties, 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 the 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 40 CFR part 158 requirements of the 1984 regulations. Additional data for

older pesticides were called in where gaps in the scientific data base occurred. The Agency has 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 exemptions, FIFRA sec. 5 requires persons seeking experimental use of pesticides under field conditions to obtain an experimental use permit (EUP). An EUP allows limited distribution and 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 assess 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 exposure and cumulative risk 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. As previously mentioned, in 1996, the FQPA modified the 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. (In this preamble, references to tolerances include exemptions from tolerance since the standards and procedures for both are essentially the same.) 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 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 prescheduled 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 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 will 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. What is the Context for Today’s Proposal?

Under FIFRA, as previously stated, every pesticide product must be registered (or specifically exempted from registration under FIFRA section 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 registration. The establishment of tolerances, if appropriate, is part of the registration process.

### B. 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 the product 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 the 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, nontarget insect species and to determine what happens to the pesticide in soil, water, and air.

### C. What are the Data Requirements?

First promulgated in 1984, the data requirements in 40 CFR part 158 (49 FR 42856, October 24, 1984) 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,

biochemical, microbial, etc.), scientific discipline (e.g., toxicology, etc.), and major use sites (e.g., outdoor vs. indoor, terrestrial, aquatic, greenhouse). Part 158 also outlines the associated procedures for submitting the data, requesting a waiver from a requirement(s), and other associated procedures. Since there is much variety in pesticide chemistry, exposure, and hazard, part 158 is designed to be flexible. Table notes (referred to as test 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.

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. Data requirements address both components of a risk assessment, i.e., what hazards do the pesticide present, and estimated level of exposure to humans or nontarget species. 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 extensive hazard data may not be required 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 EPA 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), which includes representation of countries throughout the world (including the United States). The process for developing and amending the test guidelines included 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 provide recognized standards for conducting acceptable tests, guidance on reporting data, definition of terms, consistent with the purpose of the data requirement and the test standard and recommended study protocols. As such, pesticide registrants may also use a nonguideline 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 is expected to fully justify the methods chosen in the study protocol. Nonguideline protocols may be

accepted, provided that the study protocol meets the purpose of the data requirement 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 a <http://www.epa.gov/opptsfrs/home/guidelin.htm>. Please see the docket for the complete crosswalk for old guideline numbers to new guideline numbers (Ref. 2).

#### *D. Why have EPA's 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. During the registration process, EPA recognized that some of the 1984 data requirements were becoming out of date. The Agency then called in additional information in order to complete the registration process.

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," 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 and reproductive testing (National Research Council, 1993, pp. 152-156) (Ref. 3), which applies to biochemical and microbial pesticides. NRC also suggested adding a thyroid screen to existing subchronic and chronic toxicity tests and additional tests of 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.

3. *Scientific Advisory Panel Review of 1994*. The FIFRA SAP completed a review of a set of scientific issues regarding the Environmental Protection Agency's Proposed Rule: Pesticide Registration Data Requirements, 40 CFR part 158 (Ref. 4). The Panel commended the Agency for presenting this regulation in such a clear and understandable manner, and generally endorsed the revisions. The Panel addressed individual scientific issues where necessary for both biochemicals and microbial pesticides and the data needed to address risk.

4. *The Food Quality Protection Act of 1996 (FQPA)*. Passage of FQPA in 1996 reformed the 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. Since the early 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 nonoccupational 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 nonoccupational and residential exposure.

5. *Pesticide reregistration*. Recognizing that pesticides registered in the past may not meet today's safety standards, EPA is reviewing and reregistering older pesticides and taking action to reduce risks where appropriate. On July 13, 2005, EPA published a notice of proposed rulemaking (NPRM) to establish procedural regulations for conducting registration review (70 FR 40251, July 13, 2005), as required in FIFRA section 3(g). Registration review will replace

EPA's one-time pesticide reregistration and tolerance reassessment programs starting in 2006. The Agency will conduct a review of each pesticide at least every 15 years to ensure that registrations continue to meet statutory standards for registration. EPA plans to make decisions on almost 50 registration review cases, or about 80 active ingredients, each year. Under the reregistration process required by FIFRA section 4, EPA has been reviewing older pesticides (those initially registered before November 1, 1984) to consider their health and environmental effects and to make decisions about their future use. EPA is committed to completing the reregistration process by the end of fiscal 2008.

## V. Scope, Purpose, and Request for Comments on this Proposal

### A. General Background on the Phased Rulemaking Approach

EPA is responsible for registration of the following categories of pesticides: Biochemicals, microbial and plant-incorporated protectants, conventional pesticides, and antimicrobial pesticides. The various processes include differing data requirements that registrants must take into account in their submittals.

On March 11, 2005, EPA published a proposed rule to update and revise its data requirements for the registration of conventional pesticides (70 FR 12276) (Ref. 5). In addition to proposing specific changes to the data requirements for registration of conventional pesticides, EPA proposed a number of other changes to the general provisions of part 158. Specifically, subpart A of the proposed rule for conventional chemicals describes general provisions including definitions, format of data submissions, policies on Confidential Business Information (CBI), flagging criteria, waivers, and minor uses. Subpart B of the proposed rule for conventional chemicals describes expanded use patterns, clarifications on using the data tables, identifying data for Experimental Use Permits (EUPs), test guidelines, and purpose of the registration data requirements. That proposed rule also proposed to upgrade the structure of part 158, assigning biochemical data requirements to subpart L, and microbial pesticide data requirements to subpart M of part 158.

Today's proposed rule proposes to update and revise the data requirements for the registration of biochemical and microbial pesticides, and to maintain the structure proposed in the earlier proposed rule for conventional pesticides, by placing the proposed data

requirements for biochemical and microbial in new subparts L and M, respectively. When the proposed rule for conventional pesticides is finalized, the general provisions of subparts A and B of that rule will apply to the other data specific subparts, such as subparts L and M as proposed today, unless otherwise specified. Future rulemakings will address the data requirements for antimicrobials and plant-incorporated protectants.

### B. Summary of this Proposal

EPA is proposing a number of changes to the current data tables. The proposed rule would:

1. Codify current data requirements that do not appear in part 158, but which are routinely required.
2. Add new data requirements.
3. Revise certain existing data requirements, such as by updating test notes.
4. Clarify the definitions of both "biochemical pesticide" and "microbial pesticide" to reflect our current application of those terms, and make a conforming change in the part 172 definition of "microbial pesticide."
5. Add additional definitions needed to apply the data requirements properly.
6. Make necessary reorganizing and formatting revisions, such as renaming data requirements.

EPA will retain its current tiering system for both biochemical and microbial pesticide data requirements.

### C. What are the Purposes of this Proposal?

EPA has a number of objectives in proposing this regulation to update and revise the data requirements in 40 CFR part 158.

1. *Ensuring high quality data to meet EPA's mandates*. Although most of the specific requirements in part 158 have not changed since the data requirements were first published in 1984, aspects of the requirements may be out of date or may be unclear because the underlying science has advanced (e.g., National Academy of Sciences (NAS) in 1993 suggested changes to better protect children) or the Agency's legislative mandate has been broadened to address new concerns. For example, given the stricter mandates imposed by the 1988 FIFRA amendments and the 1996 FQPA amendments to FIFRA and FFDCA (emphasis on exposure to population subgroups), 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.

In light of this background, the primary purpose of this proposal is to

transparently identify the data EPA needs and will require to support a determination of “reasonable certainty of no harm” under FFDCA and “unreasonable adverse effects” determination under FIFRA. In developing this proposed rule, EPA has evaluated its data needs to conduct the expanded risk assessments required by new statutory mandates. Thus, the proposed changes entail both new tests and broadened requirements for some current tests, reflecting the changes in data requirement practices that have evolved since the 1984 data requirement rule was promulgated and addressing data needed to meet requirements created by statutory amendments to FIFRA and FFDCA.

2. *Ensuring a sound scientific basis that is consistent with advances in scientific understanding and works toward harmonization to avoid duplicative data.* Relatedly, these proposed revisions are intended to ensure that the data requirements in part 158 reflect current scientific understanding and scientific advances since the data requirements were first issued in 1984. As discussed throughout this document, these proposed revisions have been presented to, and reflect the advice and recommendations of, the NAS and FIFRA SAP. Issues and related materials that are brought by EPA to the FIFRA SAP undergo a public review and comment opportunity before the FIFRA SAP issues its report with recommendations to the Agency.

To the extent feasible, the proposed revisions are a reflection of the scientific advances within OECD countries. The United States participates in OECD activities to harmonize international testing standards and, where appropriate, reference to the OECD testing standards have been included in this proposal. However, since EPA continues to allow applicants to submit and use their own study protocols consistent with the purpose of the requirement to generate data that they subsequently submit to EPA, and there are differences in the mandate and authorities between EPA and the governing authorities within OECD countries, the data submitted to EPA under part 158 would be expected to satisfy OECD testing standards under most circumstances for microbial testing (because OECD has agreed to use the U.S. microbial pesticide testing guidelines) and for a number of countries some of the U.S. biochemical testing guidelines would be satisfied. A few of the governing authorities within the OECD countries may want additional studies that would not normally be required in the United

States, but protocols for these studies are generally acceptable to all countries.

3. *Improving the depth and transparency of 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 improve the depth and transparency of the Agency’s understanding of the health and environmental effects of pesticides to which individuals and the environment may be exposed. For example, the proposed rule includes a test note for the human health assessment data requirements indicating data are not required to support straight chain lepidopteran pheromones when used at certain application rates. In addition, EPA is proposing to continue using the tiered testing system, as given in the current §§ 158.690 and 158.740, since many of the higher tiered data will not be required unless the results from the lower tiered studies indicate a concern for adverse effects.

4. *Improving utility of the part 158 data tables.* As described in the Notice of Proposed Rulemaking on Conventional Pesticides (70 FR 12276, March 11, 2005), EPA has proposed to reorganize and reformat part 158 subpart A (General Provisions) and subpart B (How to Use Data Tables), and reorganize and redesignate subpart D (Data Requirement Tables) into several individual subparts (see Table 1 in Unit VI). In the proposed reorganization, subpart L is designated for biochemicals (§ 158.900) and subpart M (§ 158.1000) is designated for microbials. Within both subpart L and M, there are definitions, examples, applicability, and then the series of data requirements in tables addressing product chemistry, residue chemistry, human health assessment or toxicology, nontarget organism, and environmental fate.

Many of the revisions proposed in this document are intended to improve the usefulness of part 158 data tables by better 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.

5. *Reducing burdens where consistent with need for data.* In proposing new and revised data requirements, EPA expects that fewer data waivers will be needed where the issue is well resolved, e.g., straight chain lepidopteran pheromones (SCLPs), and physical chemical properties criteria outlined in

test notes when data are not required. There are also more transparent test notes indicating when data are required, while providing assistance to avoid generation of data where unnecessary. There is also an opportunity to reduce cost of preparation of waiver requests by providing pre-submission/post-submission meetings where appropriate.

*D. What are Some of the Benefits of this Proposal?*

Discussed in more detail in the document entitled “Economic Analysis of the Proposed Change in Data Requirements Rule for Biochemical and Microbial Pesticides,” which is available in the docket for this rulemaking (Ref. 6), the following briefly highlights the benefits anticipated from this proposal:

1. *More refined assessments mean clearer understanding of real risks.* EPA’s current applicator/user exposure data base is not comprehensive, especially regarding exposures to pesticides in nonagricultural settings. The new data that would be collected under this proposal would allow the Agency to conduct improved exposure assessments for applicators/users (i.e., especially for insect repellents). This will benefit growers, other workers, and consumers by allowing EPA to make better informed regulatory decisions that are neither too stringent nor too lenient.

2. *Clarity and transparency to regulated community means savings.* The enhanced clarity and transparency of the information presented in part 158, subparts L and M 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, thereby registering safer pesticides sooner and potentially reducing risks as well as 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 and nonagricultural products and registered pesticides as tools for public health.

3. *Enhanced international harmonization means less duplication.* EPA participates with OECD countries in the development of harmonized international standards and, to the extent possible, we have included these revisions in our proposal. The OECD Biopesticide Steering Group has agreed to use U.S. EPA Harmonized Guidelines for the conduct of microbial pesticide studies and we continue to work

together to harmonize our approach to evaluating and reviewing these data. However, because other OECD countries do not use the tiered approach to the data requirements, but instead decide on the data needed for registration on a case-by-case basis, there may be differences in the actual data required for registration for the United States compared with other OECD countries. We are presently working with key OECD biopesticide regulatory representatives to develop OECD guidance for waiving data, which will bring actual data requirements closer together. OECD has also recognized pheromones, a certain type of biochemical pesticide, as warranting a separate, unique set of reduced data requirements similar to the U.S. data requirements.

4. *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 nontarget 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.

5. *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/users) 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.

#### *E. How will this Proposal Affect Existing Registrations?*

- This proposal codifies existing practices by requiring data that are necessary to complete a risk assessment that are not included in the current data requirements.
- This proposal imposes new requirements for future registrations, as is the case for applicator/user exposure data to assess impacts from insect repellents.
- In rare circumstances, the Agency may find it necessary to call in data on certain existing registrations, as warranted by emerging risk issues.

#### *F. Request for Comments*

The Agency invites the public to provide its views on the various options proposed or present any data or information for the Agency to consider during the development of the final rule. Specifically, the Agency welcomes specific comments on the following topics of particular interest to the Agency.

The Agency welcomes specific comments on the need for, value of, and any alternatives to, the data requirements described in this document to meet its mandates.

The Agency welcomes comments on the scientific basis of this proposed rule.

The Agency welcomes specific comments on the clarity of the proposed data requirements for biochemical and microbial pesticides and the relationship between the proposed data requirements and EPA's statutory determinations.

The Agency welcomes specific comments on the transparency of the proposed definitions, examples, and applicability for both biochemical and microbial pesticides.

The Agency welcomes comments on its economic analysis of the proposed rule, as well as on its underlying assumptions, economic data, and high- and low-cost options and alternatives. Describe any assumptions and provide any technical information and data used in preparing your comments. Explain estimates in sufficient detail to allow for it to be reproduced for validation. 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 biochemical and microbial pesticide applicants.

## **VI. Background on Regulation of Biochemical and Microbial Pesticides and Preparation of this Proposed Rule**

### *A. Background of Regulating Biochemical and Microbial Pesticides*

The Agency finalized the data requirements to support the registration of biochemical and microbial pesticides (49 FR 42856, October 24, 1984) more than 20 years ago. When promulgated in 1984, EPA distinguished "biochemical and microbial pesticides" from "conventional chemical pesticides" by "their unique modes of action, low use volume, target species specificity or natural occurrence." EPA recognized that biochemical pesticides are inherently different from conventional pesticides since they are generally naturally-occurring and have a non-toxic mode of action.

As a result, biochemicals are expected to pose lower potential risk compared to conventional pesticides. Due to the non-toxic mode of action and low risk to humans, certain studies are not included in the Tier I data requirements for biochemical pesticides. This adjustment in the tiered data requirements was intended to serve as a safety mechanism. If Tier I testing indicates a toxic mode of action, the biochemical would be treated as a conventional pesticide, and virtually the same toxicology and residue data would be required as is required for a conventional pesticide.

The Agency has confirmed in the past 20 years of regulating biochemical pesticides that indeed biochemical pesticides can be classified and regulated with the data requirement tables that have been designated for biochemical pesticides. The Agency recognizes that at the time of application for registration there are instances where a biochemical may not fit the biochemical category and in such cases the Agency evaluates the pesticide in question as a conventional pesticide. Ultimately, if a pesticide were to exceed the criteria established for a biochemical pesticide, the data requirements in the higher tiers would be required and the process would take longer than if the application were made as a conventional pesticide, since all data requirements would not be clearly identified from the onset.

Microbial pesticides are living organisms and, as such, present much different risk concerns than chemical toxicants. The main concern for a microbial pesticide is whether it could survive within, and be pathogenic to, a nontarget species or humans. As a result, required studies specifically address the potential for these unique

risks. Some microorganisms do produce toxins. If comparisons of the microorganisms indicates that taxonomically similar microorganisms have been reported to be pathogenic, the data set is configured to allow for use of conventional toxicity testing if needed to evaluate any toxins.

### B. History of Development of Biochemical and Microbial Pesticide Data Requirements and Guidelines

1. *Biochemical pesticides history for regulatory activities.* The following provides the history in the regulatory development of the data requirements for biochemical pesticides since 1984.

- 1984—Promulgation of 40 CFR part 158 subpart A: § 158.65 Biochemical and Microbial Pesticides and subpart D: § 158.690 Biochemical Pesticide Data Requirements and Microbial Data Requirements (49 FR 42856, October 24, 1984).

- 1987—Report of SAP Recommendations: A Set of Issues Being Considered by the Agency in Connection with Proposed Revision to Subdivision M, Immunotoxicity Testing of Biochemical Pest Control Agents (Ref. 7).

- 1989—Issuance of Subdivision M of the Pesticide Testing Guidelines Microbial and Biochemical Pest Control Agents (Ref. 8). Although titled as such, this guideline did not include a discussion on biochemical guidelines. The Agency still relies on 1982 Pesticide Assessment Guidelines Subdivision M Biorational Pesticides (Ref. 9) for the guidelines pertaining to biochemicals (880 series) if there is not a designated guideline in the conventional pesticide series (i.e., 870 series and 850 series).start here next

- 1994—Presentation to SAP to discuss data requirements for all pesticides, including biochemical and microbial pesticides (Ref. 4). Some data requirements were presented to support conventional pesticides, i.e., applicator/user exposure data to support insect repellents (Ref. 10).

2. *Microbial pesticides history for regulatory activities.* The following provides the history in the regulatory development of the data requirements for microbials since 1984.

- 1984—Promulgation of 40 CFR part 158 subpart A: § 158.65 Biochemical and Microbial Pesticides and subpart D: § 158.690 Biochemical Pesticide Data Requirements and Microbial Pesticide Data Requirements (49 FR 42856, October 24, 1984).

- 1987—Presentation to SAP in 1987 for microbial pesticides in preparation for updating the guidelines (Ref. 7) on immunotoxicity testing.

- 1989—Issuance of Subdivision M of the Pesticide Testing Guidelines Microbial and Biochemical Pest Control Agents (Ref. 8). This was a culmination of the 1987 SAP and public comments.

- 1994—Presentation to SAP to discuss data requirements for all pesticides, including biochemical and microbial pesticides (Ref. 4).

This proposed rule proposes to codify the draft data requirements outlined and presented to the FIFRA SAP in 1994 and in subsequent meetings. However, EPA is proposing certain revisions for biochemicals that are also discussed fully in the Agency's proposal for conventional chemicals (70 FR 12276, March 11, 2005) (Ref. 5). The Agency developed a complete list of data requirements for biochemicals and microbials and the year each were presented to FIFRA SAP (Ref. 11). This reference, the SAP final reports, and relevant documents presented to the SAP are available in the docket for this proposed rulemaking.

### C. EPA Activities in Preparation for this Proposed Rule

1. *Consideration of redesigning data requirement tables.* While preparing for this proposed rule, the Agency considered redesigning data requirements based on subcategories of biochemical and microbial pesticides. Each subcategory was evaluated based on mode of action and potential for risk to human health and the environment, with each subcategory requiring different data to support registration. The subcategories for biochemical pesticides were as follows: pheromones (including arthropod, lepidopteran, and straight chain lepidopteran pheromones), growth regulators (insect and plant), repellents (insect and others), and other biochemicals (which includes all other biochemicals). The microbial pesticides includes the following subcategories: protozoa, viruses, bacteria, and fungi.

In the economic analysis for this proposed rule, the Agency analyzed the test cost data submitted based on each subcategory to determine the different data requirements (Ref. 12). Based on the analysis, the Agency decided it was more appropriate to make the test notes more clear and transparent, and only update the data requirement tables without redesigning them based on subcategory.

2. *Consistencies between current part 158 and proposed part 158 design of data requirement tables for biochemical and microbial pesticides.* EPA is proposing to continue using the tiered testing system, as given in the current § 158.690 and § 158.740. For these

specific types of pesticides, it is appropriate to ask for studies in a tiered scheme because many of the higher tiered data will not be required unless the results from the lower tiered studies indicate a concern for adverse effects.

### 3. Consultations with stakeholders.

During the pre-rulemaking process, the Agency actively sought consultations with industry, academia, and non-profit organizations (i.e., environmental groups) on the current regulatory requirements for data and requested input on the universe of possible changes to the regulatory text. For parties interested in discussing the development of this rule with EPA, consultations were held in-person, by telephone conference, and via-email. During these pre-proposal stage consultations, the Agency did not request feedback on the changes being proposed today, whether the proposed changes are newly imposed, newly codified data, or revisions to existing data requirements. Feedback from these consultations included the following topics: existing data requirements, industry burden in fulfilling data requirements, tiered testing approach, and issuance of guidance specific to test protocols. All the stakeholder comments are available in the docket (Ref. 13).

### D. Consultations with Applicants

In an effort to improve transparency, increase efficiencies and reduce burdens, EPA is announcing a policy to provide assistance to applicants when needed in determining what data or information are appropriate to support registration of a biochemical or microbial pesticide. EPA is encouraging applicants to request pre-submission meetings to discuss these data issues. EPA is also announcing its intent to provide assistance to applicants in some narrow circumstances in preparation of an applicant's data waiver after submission of an application.

EPA notes that applications for biochemical and microbial pesticides frequently involve substances that present low risk (i.e., naturally-occurring, non-toxic mode of action, minimal exposure). Data requirements—even as proposed—may overstate the Agency's need, or may be satisfied by existing data in the open literature or other available data or information. In some cases, the applicant may not be aware of a potential rationale for a waiver or be able to identify available data or information that may satisfy a data requirement in lieu of generating new data. Thus, EPA encourages applicants to seek pre-submission meetings to discuss the appropriate data or information to support their product



and the opportunity for requesting data waivers.

1. *Pre-submission process.* During a pre-submission meeting, EPA may be aware that certain data requirements are already satisfied by available data or information. Sources of existing data include public literature and/or studies submitted by another registrant, which may be cited with data compensation procedures. EPA may also be aware of sound scientific rationales that certain data requirements should not be imposed. For example, the question the required data is intended to answer might be addressed by a combination of other information or data, and therefore might be able to be waived. In either case, during the pre-submission meeting, EPA would discuss with the applicant the grounds for citing other information or data to conclude that a data requirement has been met or the grounds for requesting a waiver where other information or data otherwise addresses the need for a specific piece of data required by the regulations have been satisfied. The applicant may then submit an application based on the discussion with EPA. The application should include a signed copy of the minutes of the pre-submission meeting listing each data requirement and the reason why EPA and the company believe a waiver is appropriate. The applicant is encouraged to submit a copy of the pre-submission meeting minutes to EPA for concurrence prior to submission of its application for a waiver.

To some extent, EPA currently offers this assistance to applicants and is simply encouraging applicants to request pre-submission meetings and suggesting a process for ensuring consistent reflection of discussions at the pre-submission meeting.

2. *Post-submission process.* Even after submission of an application for registration, EPA may find that either of these scenarios exist (i.e., basis for citing to other data/information or waiver of a data requirement). Again, EPA may discuss these issues with the applicant and the applicant may choose to amend its application by citing to other data/information or requesting a waiver.

EPA is also announcing its intention to assist applicants in the actual preparation of a data waiver in some narrow circumstances. Specifically, in the course of reviewing an application, EPA may find that in its judgment, data otherwise required by part 158 would not be necessary to grant the application or are available from other sources. EPA would notify the applicant and explain the basis for its belief in writing. If the data are compensable or exclusive in

use, the applicant may submit EPA's letter with the appropriate offer to pay or an authorization, as an amendment to its application. If the Agency explains in its correspondence that the data may be waived, the applicant may use EPA's correspondence to support a waiver request by signing the correspondence and submitting it as an amendment to its application. Because the correspondence only includes citation or discussion of existing data or information, EPA is proposing not to consider such amendments to an application to be "data" subject to the formatting provisions of § 158.32(a) as proposed on March 11, 2005 (70 FR 12276).

This pre-submission and post-submission process for ensuring that the data requirements are either satisfied or waived is specific to the review of biochemical and microbial registration applications, due primarily to the specific nature and circumstances unique to these pesticides (e.g., information already known to the Agency) and thus the Agency does not anticipate this process being widely applicable to other types of pesticides, such as conventional or antimicrobial pesticides.

EPA notes that in providing this assistance during the pre-submission and post-submission process, it will only consider readily accessible information, such as information found in Agency databases, and will not search for applicable information, data, or literature. Further, although intending to help applicants in supporting their applications, EPA does not encourage applicants to rely on this process to fill informational data gaps; doing so may be at the expense of timely review or may ultimately result in rejection of an application or petition.

Finally, providing assistance in this manner does not effectively allow applicants to circumvent the data requirements or the requirement to submit a waiver of a data requirement. The applicant must at all times submit the waiver request; EPA is simply providing assistance in what requirements are likely to be waived for a particular product or, in some narrow circumstances, assistance in the preparation of the waiver request. Throughout these mechanisms EPA is flexible in implementing the regulation. Thus, the waiver provisions currently codified and the recent proposed amendments to the waiver provisions do not need to be amended.

One of the benefits of providing this pre-submission and post-submission assistance is the reduction in burden. Prior to finalization of this proposed

rule (e.g., codifying that some data may no longer be required or adding conditions that result in data not being required), the number of opportunities for requesting waivers or citing to existing data will not change. Thus, providing assistance in this manner prior to finalization of this proposed rule may avoid the generation, processing and review of unnecessary data, and thereby ultimately save the Agency and applicant expenses, while providing the same level of protection for human health and the environment. In addition, although this proposal attempts to refine the test notes in order to be more transparent when data are required and necessary to support registration, there will continue to be opportunities to reference existing data or information or request waivers based on information that may be readily accessible to the Agency, and again avoid the generation, processing, and review of unnecessary data or information. Thus, the Agency expects to reduce burdens on both the applicants and EPA during and after the rulemaking process.

#### *E. Agency Coordination with the APHIS Permitting Process*

As a result of the comments received during the Interagency review process, the Agency and USDA have discussed the registration process of microbial pesticides and the need for coordination when an Animal and Plant Health Inspection Service (APHIS) movement permit under 7 CFR part 340 is required by USDA. USDA suggested that the registrants should be required to submit a copy of the applicable APHIS permits as part of the registration application to EPA. The Agency is seeking public comment on the most appropriate method to ensure APHIS permitting and EPA registrations are coordinated. In particular, EPA is interested in your specific suggestions on whether there should be a requirement for pesticide registration applicants to include copies or otherwise attest to the applicability of and their compliance with the APHIS requirements when they submit their registration application to EPA.

#### *F. Differences Between the Proposed Biochemical Data Requirements and the Proposed Conventional Data Requirements*

There are several revisions that were included in the proposal to amend part 158 for conventional pesticides, but were considered not appropriate for biochemical pesticides. For example, neurotoxicity studies (including acute, subchronic, delayed, and developmental neurotoxicity studies; OPPTS Test

Guidelines 870.6100, 870.6200, 870.7620, etc.) are required to support conventional pesticides. In addition, the recent proposal (70 FR 12276, March 11, 2005) identifies developmental neurotoxicity to be critical in some cases. If the Agency identifies a biochemical pesticide to be a potential neurotoxicant, then the Agency would evaluate the pesticide as a conventional pesticide, and it would then require the neurotoxicity data to support registration. The Agency prepared an overview of the proposed data requirements for biochemical pesticides as compared to conventional pesticides (Ref. 14).

#### *G. Similarities Between Both Biochemical and Microbial Proposed Rule Development and Proposed Rule for Conventional Pesticides*

The Agency proposes to retain certain data requirements when they are appropriate. For instance, biochemical pesticides data requirements for product chemistry are the same as is required for conventional pesticides (§ 158.320 through § 158.355).

Certain revisions for proposed conventional pesticides (70 FR 12276, March 11, 2005) were considered appropriate for biochemicals and/or microbials and are included in this proposed rule, i.e., registrations introducing significant exposure require applicator/user exposure data. As previously mentioned, the consistent designation of CR and R within the data tables remains the same as it is in the current part 158 for both conventional pesticides and microbial and biochemical pesticides. The proposed conventionals retains the CR and R designation, and this proposed rule retains this designation as well, within the data tables.

#### *H. Proposed Amendments and Reference to Harmonized Guidelines*

The following units VII and VIII identify the proposed revisions to the current data requirements for biochemicals and microbials. In each preamble unit, the Agency explains the basis for the proposed amendments and for ease of reference to the public, identifies the harmonized guideline that is applicable to the proposed data requirement. EPA is not proposing changes to these harmonized guidelines as they have gone through a public review. The reference is simply for ease in understanding the proposed revisions.

### **VII. Biochemical Pesticide Data Requirements (Subpart L)**

#### *A. Definition of Biochemical*

The Agency is proposing to revise the definition of biochemical. Although the current definition provides examples of biochemicals, it does not really explain what a biochemical is. The language in the current definition was constrained by the need for including microbial pesticides in the same definition that defined biochemical pesticides. The new format for this regulation allows for a separation of the two classes of pesticides. The proposed definition of biochemical is intended to reflect a more useful and transparent definition, in accordance with the original scientific rationale for creating the biochemical class of pesticides while being consistent with the examples. The current definition is listed in § 158.65 and reads as follows:

Biochemical and microbial pesticides are generally distinguished from conventional pesticides by their unique modes of action, low use volume, target species specificity or natural occurrence. ... (a) Biochemical pesticides include, but are not limited to, products such as semiochemicals (e.g., insect pheromones), hormones (e.g., insect juvenile growth hormones), natural plant and insect regulators, and enzymes. When necessary the Agency will evaluate products on an individual basis to determine whether they are biochemical or conventional chemical pesticides.

EPA is proposing to relocate the definition of biochemical to § 158.900, which would immediately precede the data requirements in part 158 for the respective categories of biochemicals. EPA is also proposing to amend the definition so that it would state the following:

A biochemical pesticide is a pesticide that:

- (1) Is a naturally-occurring substance or structurally similar and functionally identical to a naturally-occurring substance;
- (2) has a history of exposure to humans and the environment demonstrating minimal toxicity, or in the case of a synthetically derived biochemical pesticides, is equivalent to a naturally-occurring substance that has such a history; and
- (3) Has a non-toxic mode of action to the target pest(s).

EPA is proposing to continue the requirement that a biochemical pesticide be naturally-occurring. In addition, based on a long established policy, EPA is proposing to include a clarification that a "naturally-occurring" biochemical pesticide may be synthetically produced if it is "equivalent" (structurally similar and functionally identical) to the naturally-occurring chemical. A synthetically derived chemical may often be more

pure or economically feasible to produce but have the same properties as its naturally-occurring equivalent. An example of a synthetic substance that meets the criteria for classification as a biochemical is an insect pheromone manufactured by man. These insect pheromones are structurally and functionally identical to the substances that are produced by the insects, but the currently registered products are not naturally-occurring because it would be very difficult to extract them directly from an insect in a usable form.

Second, the current regulation does not explicitly indicate that inherent non-toxicity is a means of defining a biochemical. EPA is proposing to add a criterion to the definition of biochemical that requires that there be a history of exposure to the naturally-occurring pesticide or, for synthetically-derived pesticides, to the equivalent naturally-occurring pesticide, and that exposure demonstrates minimal toxicity. The original intent for specifying natural occurrence in § 158.65 was to allow EPA to use information derived from the pesticide's natural exposure to humans and non-target species to decide if the pesticide is inherently toxic. This is described in the 1982 Pesticide Assessment Guidelines, Subdivision M for Biorational Pesticides, section V(A)(2)(1) (Ref. 9), which states that the fact that the chemical is naturally-occurring is to be used to predict whether "these compounds are generally not innately toxic." Therefore, the criterion for having a history of adequate exposure was added in order to have confidence that if the naturally-occurring pesticide were not "innately" toxic, it would have to be present in the environment at sufficient levels and locations to predict significant exposure to humans and/or non-target species. If the pesticide is naturally-occurring but inherently toxic, EPA would use the data requirements for the conventional pesticides to ensure it could conduct an adequate assessment of the risks from the proposed use of the pesticide.

Thus, rather than giving the impression that natural occurrence alone defines whether the pesticide should be classified as a biochemical pesticide, the Agency is proposing to include the criterion that there be a history of exposure demonstrating minimal toxicity. In order to make this determination, the naturally-occurring pesticide or the naturally-occurring equivalent to the synthetically derived pesticide must be present in the environment in sufficient quantities so that if it is innately toxic, there would be a good chance that this toxicity

would already have been recognized because of its effect on humans or representative non-target organisms. EPA has often used public literature to demonstrate that the substance is either widely used, and/or widely known (supported by extensive information and low toxicity) as part of the decision whether a pesticide may be adequately reviewed using the reduced data set for biochemical pesticides. The natural occurrence of a pesticide does not necessarily mean that it has a non-toxic mode of action to the target pest. An example might be pyrethrins, which are naturally-occurring toxins that occur in chrysanthemum plants. The new criteria in the biochemical definition would clearly allow us to classify this as a conventional chemical pesticide that would be subject to the conventional pesticide data requirements, which is consistent with past Agency decisions.

Third, the current regulation refers to a unique mode of action, which is an attempt to describe the mode of action of both microbial and biochemical pesticides together. EPA is proposing to add a criterion to the definition of biochemical to better describe that the unique mode of action for biochemical pesticides must be one that is non-toxic to the target pest(s). This was the original intent for the biochemical pesticide mode of action as described in the 1982 Pesticide Assessment Guidelines, Subdivision M for Biorational Pesticides. That guideline explained in section I(A)(1) (Ref. 9) that "some of the characteristics that typically distinguish biorational from conventional pesticides are their unique non-toxic mode of action, ..." and in section V(A)(2)(1) that a characteristic of biochemical pesticides is that "their pesticidal action is not the result of target organism toxicification." Thus, the third element of the definition adds that the biochemical must have a non-toxic mode of action to the target pest. This toxic mode of action criterion would preclude pyrethrins and other clearly toxic naturally-occurring pesticides from being classified as biochemicals.

In addition to the proposed language noted previously, EPA is proposing to amend the examples provided in the current definition of biochemical to better represent the kinds of biochemical pesticides we have actually seen since the original rule was published and move the examples from the actual definition to a subsequent paragraph. The proposed definition removes hormones from the example list because hormones fall into the growth regulator class, which is already in the list. The new "Examples" section is proposed to read as follows:

Biochemical pesticides include, but are not limited to: (1) Semiochemicals (e.g., insect pheromones and kairomones), (2) natural plant and insect regulators, (3) naturally-occurring repellents and attractants, and (4) enzymes.

At the present time, the Agency will review requests for classification as a biochemical pesticide, but does not believe this needs to be part of the regulatory language because the proposed revised definition is much more definitive than the current definition.

As a final note, although not always the case, EPA recognizes that biochemical pesticides tend to have a limited range of target species, are often effective against their target pest(s) in relatively low quantities, and usually decompose rapidly after application in the environment.

#### *B. Applicability of Biochemical Pesticide Data Tables*

EPA is also proposing to use table descriptors NR (not required), R (required), and CR (conditionally required) to be used as markers along a spectrum of the likelihood that a data requirement applies. In other words, it should be assumed that a required (R) data requirement is required typically all the time. There may be some narrow or rare conditions identified in test notes when data are not required. For example, acute oral toxicity data are required to support registration for biochemical pesticides unless the proposed pesticide is a gas or highly volatile (which is rare). In contrast, a conditionally required (CR) data requirement is less likely to be triggered compared to a required (R) data requirement. Conditionally required data are more likely to include test notes indicating conditions when data are typically required. For example, the 90-day dermal toxicity test is currently conditionally required (CR) for biochemical pesticides. The test note indicates it is required (R) to support uses involving purposeful application to human skin or which would result in comparable prolonged human exposure to the product (e.g., insect repellents). Specific criteria are identified with the test note.

#### *C. Product Chemistry Data Requirements*

1. *General.* The Agency uses product chemistry information to determine whether impurities of toxicological or environmental concern are present in biochemical pesticides and their formulated products. Product chemistry data requirements include product identity and composition, the physical

and chemical characteristics of data on the pesticide, the identity of any intentionally added ingredients, and impurities in the final pesticide product.

The Agency is continuing to list the data requirements in the table for product identification, description of starting materials, production and formulation process, discussion of formation of impurities, preliminary analysis, certified limits, and physical and chemical characteristics, as currently listed in § 158.690. The following is a discussion about the changes from the current data requirements to support "biochemical product analysis data requirements" to the proposed "biochemical product chemistry data requirements" for biochemicals. The revised title of the proposed table more accurately reflects the current types of data required to support biochemical pesticides.

In addition, the proposed rule for conventional pesticides (70 FR 12276, March 11, 2005) identifies the following sections where this proposed rule will also require the same information/data and are indicated in the test notes within the proposed product chemistry data requirement table: §§ 158.320, 158.325, 158.330, 158.335, 158.340, 158.345, 158.350, 158.355.

2. *Proposed product chemistry data requirements.* The Agency proposes to codify one study (particle size, fiber length, and diameter distribution) and to make minor revisions to existing data requirements to support product chemistry data requirements. The Agency is also proposing to require studies to support experimental use permits (EUPs) as well as registration for certain studies, (i.e., certified limits). In addition, certain studies (i.e., enforcement analytical method) would require a different test substance (for example, TGAI or both EP and MP). One study, which is currently required to satisfy environmental fate and expression data requirements, is proposed to be moved from environmental fate and expression to the product chemistry data requirements (ultraviolet (UV)/light absorption) table. The Agency is also proposing to delineate the physical and chemical properties into subcategories, depending on the formulation type (e.g., solid versus liquid) and provide test notes identifying conditions when data are required (i.e., flammability). In other words, the current product chemistry data requirement table lists physical and chemical properties as one data requirement, whereas the proposed rule identifies the individual studies that make up physical and chemical

properties (e.g., color, odor, vapor pressure, pH). Additional test notes concerning the physical and chemical properties identifying when each data requirement is required (i.e., solid versus liquid at room temperature, water insoluble substances ( $10^{-6}$  grams/liter (g/l)) are also included.

i. *New requirements.* None.

ii. *Newly codified requirements—particle size, fiber length, and diameter distribution.* The Agency proposes to add the conditional requirement (CR) for data on particle size, fiber length, and diameter distribution. This data requirement is proposed to be conditionally required (CR), the condition being that the test substance is water insoluble ( $<10^{-6}$  g/l) or fibrous with diameter  $\geq 0.1$   $\mu\text{m}$  (micrometer). Data from this study are needed to complete the environmental fate assessment to estimate potential pesticide drift to nontarget areas.

iii. *Revisions to existing requirements.*

a. “Certification of limits” data are currently conditionally required (CR) to support all proposed use patterns/applications, except for EUPs for nonfood crops. The Agency proposes to change the conditionally required (CR) to required (R) “Certified limits” data to support proposed use patterns to ensure we have proper product chemistry information on all registrations for enforcement purposes.start

b. *UV/visible light absorption.* The Agency currently requires (R) these data to satisfy one of the nontarget organism, fate and expression data requirements. The Agency proposes to relocate this data requirement from environmental fate and expression data tables to the proposed product chemistry data table. The endpoints measured by this data, characterization, and identification of a compound are more appropriately considered product chemistry data. This is not a new data requirement, merely a relocation. This information will be used in conjunction with the “photodegradation in water” study 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. The UV/visible light absorption spectrum will indicate whether the pesticide is absorbed in this range.

c. *Revision of names.* The Agency proposes to revise names of certain studies to correspond with OPPTS Test Guidelines (Ref. 2) and to synchronize with the name changes taking place in the updating of part 158 for conventional pesticides. The following

three name changes are proposed in this section: (1) “Product identity” to “Product identity and composition”; (2) “Discussion of formation of unintentional ingredients” to “Discussion of formation of impurities”; and (3) “Manufacturing process” to “Description of starting materials, production and formulation process.”

#### D. Residue Chemistry Data Requirements

1. *General.* The Agency is proposing to codify two data requirements which identify the use pattern under which they are proposed to be required. EPA is also proposing to consolidate the nonfood use patterns into the following four categories: terrestrial nonfood; greenhouse nonfood; forestry; and domestic outdoor, and to do so for all residue data requirements except for chemical identity and directions for use. Those will remain conditionally required (CR) for all uses. This would not change the number of times the data are required, but merely consolidate the uses that have the same data required under the same conditions.

In addition, the Agency is proposing to delete the test note stipulating data conditionally required (CR) if the application rate of 0.7 ounces was exceeded. This test note is no longer considered relevant. Therefore, all the proposed residue chemistry studies would be required regardless of the application rate. It was originally incorporated in the data requirements as explained in the October, 1982, Subdivision M guidelines (pages 31 and 32, Section VI, Residue Analysis) as an estimate of a “low application rate” since the original definition for biochemical and microbial pesticides (40 CFR 158.65) mentioned that they are generally distinguished from conventional pesticides by various characteristics including “low use volume.” The Agency has determined that the key to whether residue data (which is needed only to support a numerical tolerance) are needed for biochemical (and microbial) pesticides is toxicity, not exposure by itself.

2. *Residue data requirements—i. New requirements.* None.

ii. *Newly codified requirements—a. Nature of the residue: plants; livestock.* These data are currently not required (NR) to support indoor food use. The Agency, however, proposes to conditionally require (CR) these studies to support registration of indoor food use. There have been instances where certain biochemical pesticides are applied to food crops indoors (e.g., for treatment of stored potatoes), and these potato peels are then fed to cattle for

feed. Therefore, the nature of residues on plants is needed to determine potential residues on the treated crop. The 0.7 ounces per acre restriction is no longer a trigger for requiring the submittal of data. The Agency also proposes to eliminate “Nature of residue: livestock” to support domestic outdoor use, since the data are needed for potential food uses outside of the home, and domestic outdoor use is for porches, patios, yards, home gardens, etc. EPA also proposes to no longer require testing on Pure Active Ingredient Radio Labeled (PAIRA) but instead to use the TGAI because it is difficult to isolate pure active ingredient from a naturally-occurring substance.

b. *Residue analytical method.* This data requirement is currently conditionally required (CR) for terrestrial, aquatic, and greenhouse food use with the 0.7 ounce per acre limitation (data not required if applied at rate less than or equal to) restriction. The Agency proposes these data to be required (R) for greenhouse use and continue to conditionally require (CR) data for terrestrial, aquatic, and indoor food use but without the less than 0.7 ounce active ingredient (a.i.)/per acre/year exemption. It would remain conditionally required (CR) for indoor food use. The residue analytical method data are needed to address enforcement issues, i.e. ability to measure the pesticide.

iii. *Revisions to existing requirements—a. Chemical identity and Directions for use.* These data are currently conditionally required (CR) based on a series of conditions including if the application rate exceeds 0.7 ounces (20 grams) active ingredient per acre per year. EPA proposes not to include the application rate conditions (data required only if application rate exceeds 0.7 ounce a.i./acre/year). EPA proposes test note revisions for both the chemical identity and directions for use, but preserves one test note addressing domestic outdoor use. However, EPA is proposing to continue to conditionally require (CR) this data only for all biochemicals for which residue data are required since chemical identity and directions for use are considered to be essential to understanding the pesticide. The Agency has determined that throughout the years of registration activities for all biochemicals, the chemical identity and the directions for use information are always submitted before processing the application. The directions for use are included as part of the labeling information along with the submission.

b. *Multiresidue method.* Multiresidue methodology data are currently part of

the residue analytical method requirement. The Agency proposes to codify an existing multiresidue method study (guideline 860.1360) and designate it as a separate requirement. These data, which are currently submitted to support registration, are important in designing pesticide monitoring and enforcement programs. 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 allow analysis of as many pesticides as possible, it is clearer to list these as two separate data requirements. The test note indicates that any analytical methodology must be evaluated for its ability to detect metabolites included in the tolerance expression.

*c. Magnitude of residue data.* All the studies in this category (guidelines 860.1400 through 860.1650) no longer have the application rate of 0.7 ounces a.i./per acre/ per year exemption.

*d. Submittal of analytical reference standards.* The Agency currently conditionally requires (CR) this data as "submittal of samples" as a product analysis data requirement. The Agency is proposing to revise the name to "Submittal of Analytical Reference Standards" (guideline 860.1650) and continue to conditionally require (CR) the data. The requirement for submittal of samples was moved to the residue data requirements because it is considered a residue data requirement rather than a product analysis data requirement. Biochemical pesticides are generally of low toxicity because of their non-toxic mode of action, but, if the Agency does identify toxicity concerns, then an analytical reference standard requirement will be triggered to analyze potential residues.

#### *E. Human Health Assessment Data Requirements*

*1. General.* The current "Toxicology" data requirement is proposed to be renamed from "toxicology" to "human health assessment" to include toxicology and applicator/user exposure data requirements. 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 health risk assessment. For example, an insect repellent registration would require significantly more human health assessment data compared to a

application for SCLP. The duration of the toxicity study approximates the estimated duration of human exposure, while considering species differences in maturational milestones and overall life span.

The proposed table in subpart L (§ 158.950) contains the human health assessment data requirements EPA would rely on to identify potential hazards to humans and domestic animals for biochemical pesticides, and is expected to improve the Agency's understanding of the potential pesticide hazard to animals and humans, including subpopulations such as infants and children and possible environmental effects. This proposal retains the requirements for pesticides in current 40 CFR 158.690, as well as revisions that reflect the current practices due to FQPA implementation and the evaluation of regulating biochemical pesticides.

The Agency is continuing to require toxicity studies where use patterns indicate high exposure, such as food use biochemical pesticides, as well as exposure studies required to support certain use patterns (e.g., insect repellents). The exposure data assess exposure to both the person to and for whom the repellent is being applied as well as the person who is applying the repellent (i.e., parent to child) and it also assesses hand to mouth contact (i.e. children), which often occurs under these circumstances. Other toxicity studies, e.g., 90-day dermal, 90-day inhalation, 90-day oral toxicity for nonfood use, etc., remain as conditionally required on a case-by-case basis, depending on the category of pesticide (e.g., SCLPs, growth regulators, repellents), the patterns of use (food and nonfood), and estimated exposure and the results of lower tiered studies.

*2. Human health assessment data requirements.* The following identifies the revisions from the current "Biochemical pesticides toxicology data requirements" in 40 CFR 158.690 to the proposed "Biochemical pesticides human health assessment data requirements." The title of the data table has been revised to reflect that the primary use of the data is to assess the potential risk to humans. The proposed revised table includes the toxicology data requirements and exposure studies (the latter to support insect repellent uses). There are few new studies which are proposed which were not identified until the 1986 Science Advisory Panel discussing applicator/user exposure data requirements (Ref. 10) and conditions under which data are appropriate (except the companion

animal safety data). The following lists the individual data requirements, and what the proposed rule requires and when it requires these data. There is also a discussion on why the Agency proposes companion animal safety data in this proposed rule as well.

*i. New requirements.—a. Exposure (applicator/user).* The Agency proposes exposure studies (guidelines 875.1000 through 875.1500) to be conditionally required (CR). These data are triggered when Tier I toxicology data indicate that the biochemical may pose a hazard. The Tier II human health assessment data (toxicology and/or exposure) requirements are not required if the results from the Tier I toxicity studies indicate no expected risk. The Agency recommends that registrants consult with the Agency prior to study initiation to determine what exposure studies are appropriate based on the nature of the adverse effects seen in the Tier I data. The following are the various types of applicator/user exposure data that could be required:

(1) *Dermal exposure.* The Agency proposes to conditionally require (CR) data 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 applicator/user exposure studies employ passive dosimetry techniques which estimate the amount of a pesticide 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 using patches that absorb pesticides or by removing the material that has contacted the skin before it has been absorbed.

(2) *Inhalation exposure.* To estimate inhalation exposure to pesticide residues, the Agency proposes to conditionally require (CR) both outdoor and indoor inhalation exposure studies (guideline 875.1300 and 875.1400). It has become apparent to the Agency that insect repellents when applied often result in inhalation exposure to the user (either to the person it is being applied (e.g., child) as well as to the person applying the insect repellent (e.g., adult)) and therefore the Agency would like the flexibility to require these data for this use when triggered by results from lower tier studies or estimated exposure.

(3) *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 to

satisfy, dermal or inhalation exposure data requirements provided the human pharmacokinetics of the pesticide residue are sufficiently understood to permit calculation to determine the total internal dose. Biological monitoring offers the advantage of assessing the actual internal dose, as opposed to the estimated exposure or amount of pesticide coming in contact with the surface of the skin or available for inhalation in the lungs as measured using passive dosimetry techniques. For example, biological monitoring could consist of evaluating blood for cholinesterase activity; if it is low in a blood sample, the person may have been exposed to a cholinesterase inhibitor by any route including dermal or inhalation. Also, biological monitoring may indicate whether a given substance has been absorbed through the skin or inhaled in enough quantities to be of concern.

b. *Companion animal safety data.* Companion animal safety data (guideline 870.7200) is being proposed to be part of conditionally required (CR) special testing. This data would be triggered if the product's use would result in exposure to domestic animals through, but not limited to, direct application (e.g., topical application as in insect repellents) or consumption of treated feed. This new data requirement is based on recent Agency experiences with biochemical pesticides, specifically, that there are currently no data requirements addressing potential toxicity to domestic animal species from biochemical pesticides. Fulfillment of this conditionally required data would address such potential risk concerns. This is considered part of the human health battery of studies, as it is considered for conventionals.

ii. *Newly codified data requirements.*—a. *Hypersensitivity incidents.* Currently, the Agency conditionally requires (CR) these data when they are reported. The Agency proposes to augment this data requirement to include incidents to be reported from conditionally required (CR) to required (R) for all preregistered (EUP's) and registered products. Incidents can occur from application of an EUP as well as registered products, which, if reported, would be essential to making a well informed finding. Registrants are reminded that FIFRA section 6(a)(2) requires the submission of such information for registered products (see 40CFR part 159).

b. *Product use information.* EPA is proposing to require (R) product use information (guideline 875.1700) to provide information on how the pesticide is used and applied per day.

Data would at least include: Typical application methods, typical values for application rates, timing and number of applications per season or per year, any available surveys that provide use information for insect repellents, and other use information relevant to potential exposure following a repellent application. Such use information enables the Agency to appropriately trigger other conditional data requirements, i.e., identification of potential exposure (risk), and conduct more accurate and realistic risk assessments, thus enabling the Agency to levy appropriate limitations on use to mitigate any potential risks. This data requirement is newly codified since this information is already submitted with the label and the Agency could not complete a risk determination (estimate exposure) without the information.

c. *Test note revisions and other conditions exempting data.* The Agency is proposing to add the following conditions at the onset to Tier I, Tier II, and Tier III Human Health Assessment Data Tables: Straight chain Lepidopteran pheromones are exempt if applied at a rate less than or equal to 150 grams active ingredient/per acre/year (Ref. 15). EPA is no longer requiring these data for SCLPs because the past 20 years of scientific literature supports waiving the data. SCLP's do not pose a risk to human health when applied at a rate not to exceed 150 grams active ingredient per acre. This is consistent with current implementation, e.g., § 180.1124 requirements.

The Agency proposes to provide a test note identifying when certain data are required (acute oral, acute dermal, primary dermal irritation), unless the test material is a gas or highly volatile (vapor pressure  $>10^4$  torr). The current data tables do not specify the trigger for vapor pressure. Thus, the proposed rule provides criteria and clarity.

iii. *Revisions to existing requirements.*—a. *Primary eye irritation and primary dermal irritation.* The Agency currently requires (R) these data for MP or EP. The Agency is proposing to require (R) these data for TGAI and MP test substances since effects may result from active ingredient or other (inert) ingredients in the end-use product.

b. *Dermal sensitization.* The Agency conditionally requires (CR) "Hypersensitivity study" (152–15) in current § 158.690. EPA proposes to substitute dermal sensitization data (guideline 870.2600) and to require (R) the data, since the dermal sensitization guideline measures the same endpoints and more accurately describes the nature of the type of data required in

that it identifies dermal sensitivity. The Agency considers this information a method for accurately classifying the dermal sensitization potential of the pesticide and for determining whether any observed adverse effects are inherent to the active ingredient, or caused by the presence of other ingredients. In addition, the Agency currently requires (R) this data for MP or EP. The Agency is proposing to require (R) this data for TGAI and MP test substances since effects may result from active ingredient or other (inert) ingredients in the end-use product.

c. *Mutagenicity.* The Agency proposes to change the name of the battery of studies from "Studies to detect genotoxicity" (152–17) to specific mutagenicity studies including the following: Bacterial Reverse Mutation Test (guideline 870.5100), *In vitro* Mammalian Cell Gene Mutation Test (guideline 870.5300), and *In-vivo* Cytogenetics (guideline 870.5385 and 870.5395) (Mammalian Bone Marrow Chromosomal Aberration Test and Mammalian Erythrocyte Micronucleus Test, respectively). The Agency proposes to split existing genotoxicity data requirement (152–17) into four different data requirements. The following are proposed as Tier I requirements: Bacterial Reverse Mutagenicity (guideline 870.5100) and *In vitro* Mammalian Cell Gene Mutation Test (guideline 870.5300) are proposed to be required (R) for food uses and conditionally required (CR) for nonfood uses. The following are proposed Tier II requirements: *In vivo* Cytogenetics (guideline 870.5385 and 870.5395). Second, the proposed Tier II studies, mammalian spermatogonial chromosomal aberration and mammalian bone marrow chromosomal aberration (guideline 870.5385 and 870.5395), are conditionally required (CR) for food uses if Tier I data indicate mutagenicity. The Agency is proposing these organizational changes because the original genotoxicity data requirement was actually composed of multiple studies and the actual data requirements are more clearly described when separated as found in today's proposal. For example, the current Tier II data is required on mammals and would be unnecessary if the Tier I data shows no mutagenicity concerns. In addition, the guideline under which the old genotoxicity data requirement references is 152–17 in the 1982 guidelines and it says "Data derived from short-term microbial mutagenicity tests are required..." and it mentions gene mutations, structural chromosomal aberrations, and direct DNA damage and

repair (Ref. 9). The Agency designates these as mutagenicity tests today and the overall way the Agency cumulatively test for mutagenicity has evolved since then.

d. *Prenatal developmental toxicity.* The Agency proposes to change the name of this requirement from "Teratogenicity" to "Prenatal developmental toxicity" to better correspond with the focus of the study and current terminology. The Agency currently conditionally requires (CR) this study for Tier I. The Agency proposes to require (R) this study for Tier I for food uses since food use has the highest potential exposure to humans during pregnancy; this guideline will provide sound data if needed to address prenatal development. EPA encourages preregistration meetings to determine if the data requirement can be waived because of minimal exposure; or existing data on the product in the scientific literature indicating there is not a concern for developmental toxicity. EPA will continue to conditionally require (CR) these data for a nonfood use. EPA is also proposing to conditionally require (CR) these data on a second test species for food and nonfood uses as a Tier II data requirement based on the condition that there are reproductive effects (e.g., fetotoxicity, retarded development, structural abnormalities, behavioral abnormalities and/or death) evident in Tier I, Prenatal Developmental Toxicity (guideline 870.3700).

The Agency currently does not require a reproduction study as Tier III, and EPA is proposing to conditionally require (CR) a reproduction and fertility data requirement as a Tier III study depending on the results of the Tier I and II data requirements (i.e. subchronic toxicity, prenatal development, mutagenicity studies) in order to address potential risks that may be identified in lower tier studies.

In summary, for biochemical pesticides, the tiered principle of testing requirements for developmental toxicity is as follows: identify the hazard potential in Tier I for one species; if that study is positive, another study is required (2nd species) for use in reducing the uncertainties of species-to-species extrapolation (Tier II). If positive mutagenicity or effects on reproductive organs are observed in subchronic (Tier II) studies, then the reproduction study (Tier III) would be required for greater certainty in risk characterization.

e. *Immunotoxicity.* The Agency currently requires (R) Immune Response data (152–18). The Agency has renamed the guideline name and number to

Immunotoxicity (guideline 880.3550) and is proposing to conditionally require (CR) such data as part of Tier II, with a test note indicating this data is required if there are effects on hematology, clinical chemistry, lymphoid organ weights and histopathology observed in the 90-day studies, or if the results of the Tier I mutagenicity tests are positive. The proposed change would make it consistent with current evaluation process for determining if a pesticide is expected to pose immunotoxicity. This is consistent with the Office of Pesticide Programs historic waiver of this requirement for SCLP's, as well as when there are no effects on hematology, clinical chemistry, lymphoid organ weights, etc. or when there is no evidence of mutagenicity concerns in Tier I data.

The Immunotoxicity study (guideline 880.3550) provides information on health hazards likely to arise from subchronic exposure to a pesticide, usually after dosing by the oral route (emphasis added). Tests are selected to provide quantitative and qualitative data on the capacity of a pesticide to adversely affect components of antibody-mediated and specific and non-specific cell-mediated immunity. This purpose suggests that the oral route is preferred, but the conditions for requiring immunotoxicity testing indicate that any route that is relevant to each pesticide's use pattern (primary route of exposure under conditions of use) is acceptable. (Results from one insect repellent study that was done by the dermal route *p*-menthane-3,8-diol (Ref. 16) did not show any effects on the immune system.)

EPA is also proposing to rename and move a Tier II immune response data requirement (152–24) to a Tier III data requirement (immune response guideline 880.3800). The Agency proposes to continue to conditionally require (CR) these data depending on the results of the study completed to satisfy the Tier II Immunotoxicity data requirement. The Agency believes these data address the endpoints more suitably than the results found in the Immune Response Study.

In summary, the Agency decided to raise the level of tiers for the required immunotoxicity data from Tier I to II and from Tier II to Tier III, based on the triggers used to require the immunotoxicity data. In other words, the results of the 90 day studies requested under Tier I may trigger Tier II immunotoxicity studies, but the Agency would not be able to make that determination until the data from Tier I was reviewed. This is different from

what was proposed in conventional pesticides (70 FR 12275, March 11, 2005), which requires the data (though not the same guideline (conventional pesticides requires guideline 870.7800)), since it is proposed to be required as Tier I. The Agency discussed the variability, and decided for biochemical pesticides, given their low risk, it was appropriate to defer until the data in Tier I are reviewed and determined if there was a potential for adverse effects to the immune system.

f. *Carcinogenicity.* The Agency proposes to change the name of the "Oncogenicity study" to "Carcinogenicity study" (guideline 870.4200) to reflect current terminology.

g. *90 Day–Oral Subchronic Testing.* The Agency currently conditionally requires (CR) these data for food uses. The Agency is proposing to require (R) these data for food uses since people eat food for periods longer than one day, and since biochemicals have a non-toxic modes of action, there is a need for some data comparable to dietary exposure to assure us that nothing adverse is likely to happen when there are higher than normal levels of the biochemical in our food. For instance, eating too much of a given vitamin can be toxic or too much of an essential element like iron can have some unpleasant effects.

#### F. Nontarget Organisms and Environmental Fate Data Requirements

1. *General.* The Agency uses a tiered system of ecological effects and environmental fate testing to assess the potential exposure and 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. Laboratory tests provide a screening tool for what can potentially occur in the field, whereas the field study data indicate the potential adverse effects in the field. 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 (e.g., Tier II, Tier III, and Tier IV) are needed. Tier I ecological effects testing generally consists of the basic data requirements that are necessary to determine the acute toxicity to nontarget fish, invertebrate, plant, and wildlife species. Tier II environmental fate data requirements (there are no Tier I environmental fate data requirements) revolve around the characterization of the pesticide in the environment, e.g., hydrolysis, soil and aquatic metabolism

rate, photodegradation rate in soil and water, etc.

Higher tiered studies may be conditionally required when basic Tier I data indicate there is potential for adverse effects to nontarget species. Tier II data requirements include an array of environmental fate data requirements and subchronic/chronic ecological effects tests to further refine the potential for exposure and/or risk to the environment. Tier III data requirements include a further array of field studies that address ecotoxicity concerns for terrestrial and aquatic animal species as well as nontarget plants and insects. These data provide a foundation for ecological risk assessment, which allows the Agency to determine any appropriate precautionary statements or mitigation measures necessary to support registration concerning toxicity or potential adverse effects to nontarget organisms (including endangered species).

With respect to some of the environmental fate data requirements, the Agency is providing two sets of guideline numbers where needed, the first guideline numbers are what are currently used by the Agency. The second set which are in parentheses are guidelines the Agency has in draft stage and hope to finalize in the near future. To avoid confusion on the types of data that are required, both numbers are provided for each data requirement as an interim measure until the guidelines are finalized.

**2. Nontarget organisms and environmental fate data requirements.** The Agency is proposing to add the redwing blackbird, *Agelaius phoeniceus*, to the list of species that may be substituted for the other species (i.e., mallard or bobwhite quail). This test species could be used for the avian oral toxicity study because current data requirements do not adequately characterize the risks that pesticides pose to songbirds. Other changes include revisions in the test substance, conditions under which the test is conducted, and clarification of test notes.

i. *New data requirements.* None.

ii. *Newly codified data requirements.*

a. *Regulatory text revision.* The current part 158 for biochemicals does not include regulatory text provisions within the data table section discussing the exemptions of data to support arthropod pheromones (§ 158.960(a)(2)). The Agency is proposing the following language to be part of the regulatory text in the proposed rule:

(2) The data in this section (§ 158.960) are not required for arthropod pheromones when

applied at up to a maximum use rate of 150 grams active ingredient/acre/year except when the product is expected to be available to avian species (i.e. granular formulation).

It makes it clear from the onset under what conditions these data are required. Based on a survey of data and the literature since 1984, EPA believes that arthropod pheromones pose minimal risk to nontarget species when applied at this rate or less (Ref. 15). As a result of this finding, EPA has historically waived these data and is revising the test note to reflect the current practice.

b. *EP testing.* Where nontarget and environmental fate data are required, the Agency currently requires (R) that the TGAI be used as the test substance, and does not generally require (R) or conditionally require (CR) the EP to be tested. EPA is proposing to conditionally require (CR) EP testing when any end-use formulation may contain other ingredients that may be toxic to nontarget organisms or to support arthropod pheromones that would be available to avian wildlife (e.g., granular product).

c. *Anerobic aquatic metabolism (162-3 or guideline 835.4400) and anerobic soil metabolism (162-2 or guideline 835.4200), are currently not required (NR).* The Agency is proposing to conditionally require (CR) anerobic soil metabolism for terrestrial use and anerobic aquatic metabolism for both terrestrial and aquatic uses. The Agency believes that anerobic aquatic metabolism is necessary if the pesticide is intended for application to standing water and/or low oxygen environments, e.g., rice paddies, cranberry bogs, wetlands in natural areas and would already be required under these circumstances under typical registration practices for biochemicals.

iii. *Revisions to existing requirements.* The Agency is proposing a reduction or clarification in following five data requirements: avian oral, avian dietary, freshwater fish, freshwater invertebrate, and plant toxicity testing. The Agency is proposing to not require (NR) these studies for terrestrial uses of arthropod pheromones as defined in § 158.900. Other proposed changes are as follows:

a. *Avian acute oral (guideline 850.2100)—Redwing Blackbird.* Part 158 currently only offers two test species for testing, mallard and the bobwhite quail. The Agency is proposing revisions to the Avian Acute Oral data requirement, specifically to add an optional test species (i.e. redwing blackbird), in order to address potential exposure to passerine species in a terrestrial environment. In addition, the Agency is proposing to conditionally require (CR)

EP testing if the formulation would be available to avian wildlife, e.g., granular formulation. Testing on a passerine species (i.e., redwing blackbird) may be required (R) for outdoor uses if the use pattern lends itself to higher exposure to passerine species compared to upland game or waterfowl species. EPA is requesting comments on whether this species should replace the existing bobwhite/mallard species for a biochemical pesticide, or otherwise be presented as an optional species for the conduct of the test. If so, comments are also sought on the specific criteria to be used to determine when the testing on this particular species would be required.

In addition, the Agency is proposing to conditionally require (CR) EP testing when the following apply: when any end-use formulation may contain other ingredients that may be toxic to nontarget organisms or when the end-use formulation is used to support arthropod pheromones that would be available to avian wildlife (e.g., granular product).

b. *Avian dietary (guideline 850.2200).* Part 158 currently requires (R) TGAI testing for this data requirement. In addition, the Agency is proposing to conditionally require (CR) EP testing when the following apply: when any end-use formulation may contain other ingredients that may be toxic to nontarget organisms or when the end-use formulation is used to support arthropod pheromones that would be available to avian wildlife (i.e., granular product).

c. *Fish acute toxicity test (freshwater) (guideline 850.1075), aquatic invertebrate acute toxicity (freshwater) test (guideline 850.1010).* The Agency currently requires (R) these data for all terrestrial, aquatic, forestry, and domestic outdoor uses. The Agency conditionally requires (CR) the data for greenhouse and indoor use. The Agency proposes to add two test notes to the current standards. The first proposed test note indicates when EP data are conditionally required (CR), the second test note does not require testing for compounds which are highly volatile.

d. *Seedling emergence (guideline 850.4100) and vegetative vigor (guideline 850.4250).* Part 158 currently requires (R) these data as Nontarget Plant Toxicity testing to support terrestrial and aquatic nonfood uses and forestry uses. The Agency proposes to require (R) these data for all outdoor uses. Currently there is one test note with three conditions identifying when these data are required. The Agency is proposing to eliminate these test note conditions, but add a test note requiring



EP testing when the end-use formulation may contain other ingredients that may be toxic to nontarget plants.

e. *Nontarget insect testing (guideline 880.4350)*. Currently the Agency conditionally requires (CR) nontarget insect testing (154–11) data with two test note conditions. The Agency proposes to be more transparent and require (R) these data, for all uses except indoor use. This is because it has become apparent to the Agency throughout the years, that is appropriate to require insect testing especially with these types of biochemical pesticides, to ensure they are insect specific. In addition, the actual test guideline recommends that the guideline 850.3020 be conducted on the honeybee initially, but that additional nontarget insect species may be required. The honeybee study is required since that is what has been typically submitted and addresses the issues for risk assessments for biochemical pesticides.

f. *Sediment and soil adsorption/desorption for parent and degradates; 161–1 or guideline 835.1230, and soil column leaching (163–1 or guideline 835.1240) currently designated as adsorption-desorption*. These data are currently not required (NR) for greenhouse use. Hydrolysis (161–1 or guideline 835.2120) and Aerobic Aquatic Metabolism (162–4 or guideline 835.4300) are also not required (NR) for greenhouse use. The Agency is proposing to conditionally require (CR) these data for greenhouse use. The proposed test note is also revised to indicate all these data are conditionally required (CR) depending on the results of any of the Tier I data, not limited to environmental fate data, since it is the experience of the Agency that there may be other indicators other than exposure data which would trigger the need for these data.

g. *Laboratory volatilization from soil (163–2 or guideline 835.1410) designated as volatility in current data requirements, and Aerobic soil metabolism, 161–1 or guideline 835.4100*. The Agency currently conditionally requires (CR) these data to support aquatic uses and do not require (NR) these data to support greenhouse use. The Agency is proposing to not require (NR) these data to support aquatic uses, and to conditionally require (CR) these data to support greenhouse use. Since the exposure is in the soil, it is appropriate not to require data in the water/sediment and it is appropriate to require these data for land type use. In other words, this revision is consistent with the purpose

and implementation, as well as with the guidelines.

h. *Photodegradation on soil (161–3 or guideline 835.2410) and photodegradation in water (161–2 or guideline 835.2240) identified as Soil photolysis and Aquatic photolysis in current guidelines*. Part 158 currently conditionally requires (CR) these data for all uses except greenhouse and indoor use. That study is designed to measure photolysis of a pesticide on the surface of the soil. Water will attenuate the amount of sunlight reaching underlying sediments in a water body, thereby making photolysis of a sediment bound pesticide unlikely. In that case, measuring photolysis of the pesticide in the water column would be more appropriate. Therefore, the Agency proposes to not require (NR) photodegradation of parent and degradates in soil for aquatic (food and nonfood), since photodegradation cannot be measured in the soil under the water, but the Agency is continuing to conditionally require (CR) the direct photolysis rate of parent and degradates in water, since photolysis can be measured. The Agency proposes to add a condition for terrestrial, greenhouse, and forestry uses, when the results of Tier I studies demonstrate a concern for toxicity, and an evaluation of potential exposure (environmental fate) is needed to make a risk determination. EPA also proposes to change the names of these studies from “soil photolysis” to “photodegradation on soil” as designated in (161–3 or guideline 835.2410) and from “aquatic photolysis” to “photodegradation in water” also identified as direct photolysis rate of parent and degradates in water (161–2 or guideline 835.2240). In essence, the proposed data requirements are in line with the proposed use patterns, where the exposure is eminent.

i. *Partition coefficient (n-octanol/water) (guidelines 830.7550, 830.7560, and 830.7570)*. Part 158 currently conditionally requires (CR) this study when results from Tier 1 tests indicate environmental fate data are needed. The Agency proposes to relocate this requirement under the product chemistry data requirements. As further explained in that section of the preamble, the study would no longer be dependent on Tier I studies, but would be conditionally required (CR) for organic chemicals unless they dissociate in water or are partially or completely soluble in water.

j. *UV/light absorption (guideline 830.7050)*. Part 158 currently conditionally requires (CR) this study for all uses except greenhouse (food and

nonfood) and indoor use. As explained elsewhere, the Agency proposes to transfer this data requirement to product chemistry data requirements and to require (R) this for all 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 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. The UV/visible light absorption spectrum will indicate whether or not the pesticide absorbs in this range.

k. *Dispenser-water leaching (guideline 880.4425)*. Part 158 currently does not require (NR) this study to support greenhouse uses and indoor use. The proposed rule conditionally requires (CR) this study for greenhouse use and does not require (NR) for aquatic uses. This proposed change brings the data table in line with the guideline and only require the data when the pesticide is applied to land in a passive dispenser.

l. *Terrestrial wildlife, aquatic animal, nontarget plant, and insect testing*. The Agency currently divides Tier III studies into four categories: terrestrial, aquatic animal, nontarget plant, and nontarget insect testing. The Agency proposes to identify individual studies and their respective guideline numbers that may be conditionally required (CR) when results from lower tiered data indicate the potential need for additional studies. The test notes have not been revised, therefore the conditions under which these data are required will not be revised. However, the Agency is updating the guideline numbers. As a result guideline 850.2300 through 850.2500 apply to various terrestrial data requirements (avian and mammal), guideline 850.1025 through 850.1500 for aquatic animal data requirements (freshwater and marine fish and invertebrate species), and guideline 850.4225 through 850.4450 for nontarget plant studies.

The Agency currently conditionally (CR) requires Tier III nontarget insect testing depending on the results of the lowered testing for nontarget insects. The Agency proposes to conditionally require (CR) field pollinator testing (to address risks to bees) data (guideline 850.3040) as Tier III, if the product is expected to be transported during application to air, soil, or water, which is determined in the Tier II environmental fate studies. Based on industry information, and fate data indication potential for exposure, we

might then require some type of Tier III testing. This testing would have to be preceded by consultation with OPP, because it would be directed at the problem identified earlier. We would need to consider the species at risk, route of exposure, etc. Additional insect species may have to be tested if necessary to address issues raised by use patterns and potential exposure of important insect species, e.g., beneficial insects, endangered species. The guideline number is guideline 850.4030.

m. *Product performance.* Currently the Agency relies on § 158.640 for product performance data requirements for biochemicals and microbial pesticides. The Agency is proposing to include product performance in the regulatory text for both biochemicals and microbial pesticides to improve transparency. Product performance verification can be important, especially for public health pests, for some of the biochemical and microbial pesticides since we have seen independent reports that some do not work as well as the conventional pesticide products.

## VIII. Microbial Pesticides Data Requirements (Subpart M)

### A. Definition of Microbial Pesticide

Amendment to part 158. The Agency is proposing a revision in the definition of a microbial pesticide. The current definition at § 158.65 of microbial pesticides is:

Biochemical and microbial pesticides are generally distinguished from conventional pesticides by their unique modes of action, low use volume, target species specificity or natural occurrence. In addition, microbial pesticides are living entities capable of survival, growth reproduction and infection. ... Microbial pesticides include microbial entities such as bacteria, fungi, viruses, and protozoans. The data requirements apply to all microbial pesticides, including those that are naturally-occurring as well as those that are genetically modified. Each "new" variety of subspecies, or strain of an already registered microbial pest control agent must be evaluated, and may be subject to additional data requirements.

The definition of a microbial pesticide in the proposed rule is as follows:

Microbial pesticide means a microorganism intended for preventing, destroying, repelling, or mitigating any pest, or intended for use as a plant regulator, defoliant, or desiccant, that: (1) Is a eucaryotic microorganism including, but not limited to, protozoa, algae, and fungi; (2) Is a procaryotic microorganism, including, but not limited to, bacteria; or (3) Is an

autonomous replicating microscopic element, including, but not limited to, viruses.

This proposed definition of microbial pesticide is based on the language in the current definition of microbial pesticide at § 158.65 and the class of nonexempt biological control agents in § 152.20(a)(2), but uses a structure for defining microbial pesticide similar to that at 40 CFR 172.43. Specifically, the proposed definition replicates the structure used in § 172.43 that identifies the intent of the microbial pesticide, for example, as the prevention or destruction of a pest. The proposed definition also combines the structure and examples at § 152.20 with the current regulatory structure to clarify the intended scope of the current regulatory definition and relationship to § 152.20. For example, the proposed definition includes references to eucaryotic and procaryotic microorganisms, terms not found in the current definition at § 158.65 but found in § 152.20(a)(3). The proposed definition also clarifies that microbial pesticides include viruses and other similar infective elements, while the "autonomous replicating" language is intended to exclude pesticide components of microscopic cells that are not able to replicate as separate entities, such as genetic constructs inserted intentionally into the cells. None of these proposed amendments are intended to change the scope of the current regulatory definitions of microbial pesticide at § 158.65 or of the exemption provision at § 152.20(a)(3).

EPA is also proposing not to include in the definition of microbial pesticide the phrase from current § 158.65 distinguishing microbial pesticides from conventional pesticides because the original definition was more of a description of those characteristics that might be shared by both biochemical pesticides and microbial pesticides. In this rule, we have described biochemical pesticides separately and we can now be more specific in defining microbial pesticides.

EPA notes that microorganisms are known to produce many pesticidal substances. These pesticidal substances, when used independently of the microorganism, are considered to be biochemical pesticides, conventional chemical pesticides, or antimicrobial pesticides, depending on the mode of action and the use. The microorganism would then usually be considered part of the manufacturing process. For example, streptomycin, an antibiotic produced by a bacterium, *Streptomyces griseus*, is registered as a conventional chemical fungicide.

### B. Applicability of Microbial Pesticide Data Tables

EPA is proposing to create a new applicability provision expressly providing that the microbial pesticide data tables apply to microbial pesticides, as described previously, and to add to that paragraph specifics on the types of microbes subject to the subpart M data requirements.

First, the language in current § 158.65 states that "each new variety of subspecies, or strain of an already registered microbial pest control agent must be evaluated, and may be subject to additional data requirements." The proposed refinement now reads "each new isolate of a microbial pesticide is treated as a new strain and must be registered independently of any similar registered microbial pesticide strain and supported by data required in this subpart." This refinement is simply intended to clarify the intent of the current regulatory language.

The second sentence added to the applicability provision states that genetically modified microbial pesticides may be subject to additional data or information requirements on a case-by-case basis depending on the particular microorganism and/or its parent microorganism(s), the proposed pesticide use pattern, and the manner and extent to which the organism has been genetically modified. That language is moved from current § 158.65.

The final sentence reads "pest control organisms such as insect predators, nematodes, and macroscopic parasites are exempt from the requirements of FIFRA as authorized by section 25 (b) of FIFRA and specified in § 152.20 (a) of this chapter." That sentence is moved from current § 158.65 as well.

In addition, the current regulatory text at § 158.65 specifies that the microbial "data requirements apply to all microbial pesticides, including those that are naturally-occurring as well as those that are genetically modified." This language is not needed in the definition; the use of the data requirements for microbial pesticides is fully described in the section immediately following the definition.

Other portions of the current text at § 158.65 are proposed to be moved to the applicability subsection of subpart M, § 158.1000, or the other provision that seems generic § 158.1010 to avoid confusion on the definition of microbial pesticide. Specifically, EPA is proposing to move current § 158.65(b)(2) to proposed § 159.1010.

EPA is also proposing to use table descriptors NR (not required), R

(required), and CR (conditionally required) to be used as markers along a spectrum of the likelihood that a data requirement applies. In other words, it should be assumed that a required (R) data requirement is required typically all the time. There may be some narrow or rare conditions identified in test notes when data are not required. For example, acute injection toxicity (intraperitoneal or intravenous) not required when the microbial pesticide is a virus. In contrast, a conditionally required (CR) data requirement is less likely to be triggered compared to a required (R) data requirement, but more likely include test notes indicating conditions when data are typically required. For example, the primary dermal irritation is currently conditionally required (CR) for microbial pesticides. The test note indicates it is required (R) when dermal irritation is reported from the acute dermal toxicity study. Specific criteria are identified with the test note.

#### C. Amendment of Part 172

The Agency is also proposing to replace the definition for a microbial pesticide at 40 CFR 172.43 with the definition proposed here. The proposed definition is broader than the definition at § 172.43 in that it uses the term "includes" rather than "means" and identifies a category for autonomous replicating microscopic elements, rather than just including viruses. EPA is proposing a broader definition because it has been EPA's experience that there are microorganisms other than viruses that could be used as a pesticide but that would otherwise be excluded by the definition at § 172.43.

#### D. Product Analysis Data Requirements

1. *General.* The Agency uses product analysis information to determine whether impurities of toxicological or environmental concern are present in the pesticide and formulated products. Product analysis data requirements include product identity and composition data, physical and chemical characteristics of a pesticide, plus any intentionally added ingredients and impurities in the final pesticide product. Included in this category are the specific, detailed requirements for product identity and chemical analysis. The title of the data requirements, "microbial pesticides product chemistry data requirements," is proposed to be revised to "microbial pesticides product analysis data requirements" to better reflect the extra identification procedures necessary to analyze living organisms. The following

discussion addresses the proposed data requirements.

2. *Product analysis data requirements.* Currently, the Agency groups all the physical and chemical properties studies under one section. The Agency proposes instead to list the individual studies that are included in the category of data requirements to support registration (guideline 830.6302 through 830.7300). The Agency currently requires (R) all product chemistry data to support registration, except for analysis of samples and submittal of samples, which is proposed to be required under residue chemistry data requirements.

i. *New requirements.* None.

ii. *Newly codified requirements.*

None.

iii. *Revisions to existing requirements.*

a. Product identity, manufacturing process, and deposition of a sample in a nationally recognized culture collection. Currently these data are required as guideline numbers 151–20, 151–21, and 151–22. The Agency proposes that these data requirements would remain the same as before. However, we are proposing to list each as a separate study: product identity; manufacturing process; and, discussion of formation of unintentional ingredients. The Agency proposes to list them as follows: product identity (guideline 885.1100), manufacturing process and deposition of a sample in a nationally recognized culture collection (guideline 885.1200), and discussion of formation of unintentional ingredients (guideline 885.1300).

b. *Physical and chemical characteristics.* The Agency currently requires (R) physical and chemical characteristics data. The Agency proposes to require (R) that the same studies and same endpoints be evaluated, however the Agency is trying to be more clear by identifying the individual pieces of the data requirement and separately identify each in the data table. Specifically the studies are identified as: color, physical state, odor, stability, storage stability, miscibility, corrosion characteristics, pH, viscosity, and density (guidelines 830.6302 through 870.7300).

c. *Analysis of samples.* This study (guideline 885.1400) is currently conditionally required (CR) for EUPs and registrations. The Agency proposes to revise this data requirement to be required (R), since it is critical to have an analysis of samples to understand the composition of the microbial pesticide and the potential for contamination with other microorganisms.

d. *Certification of limits.* This study is currently required (R) except for

nonfood uses. The Agency is proposing to expand this data requirement to be required (R) for all uses. These studies are needed to confirm the claims made on the label and to validate the confidential statement of formula.

e. *Analytical methods.* The analytical methods would typically assure that you could quantify the confidential statement of formula. This study is currently required (R), and the Agency proposes to continue to require (R) these data, but under product identity and discussion of unintentional ingredients data requirements, which provide these data.

f. *Submittal of samples.* This provision is typically intended to enable EPA to identify the active ingredient and provide standards to governmental agencies needing to monitor chemical pesticide residues and is conditionally required (CR). The Agency proposes to require (R) these data as a product analysis requirement to be deposited in a nationally recognized culture collection to allow EPA to validate strain identity if issues arise (guideline 885.1200).

Since the Agency does not have capacity to store the variety of microbial pesticides that may be submitted, EPA did not set up a nationally recognized culture collection. There are several nationally recognized culture collections in this country (and abroad) such as the American Type Culture Collection and a microbial collection maintained in Peoria, Ill., by the USDA. These facilities have a vast number of microbial and cell cultures that are dedicated to transferring, maintaining and identifying. Rather than duplicate this effort, EPA chose to refer microbial pesticide producers to these facilities who have the routine expertise to keep and distribute (or protect) microbial cultures. There is a certain element of required expertise but really the cost and small number of our microbial pesticides would make it prohibitively expensive for the Agency to do this collection rather than direct the companies to these specialized facilities.

#### E. Residue Chemistry Data Requirements

1. *General.* The Agency uses residue chemistry information to determine the potential bioavailability of pesticide residues on food. Included in this subpart are the detailed requirements for chemical identity, analytical methods for plants and animals, nature of residue, stability, and magnitude of residue.

2. *Residue chemistry data requirements.* The residue chemistry

data table currently requires residue data under one data requirement. The Agency is proposing to delineate the residue data to clearly identify the endpoints being measured. In other words, there is only one data requirement, and in the proposed rule there are several data requirements listed (guideline 885.2000 through 885.2350), but no more additional data are actually required. In addition, the current test note in part 158 delays the residue study requirement until Toxicology Tier II and Tier III data are required (R). The Agency is proposing the data requirement not be dependent on the Tier Data in II and III, but to conditionally require (CR) these data when the results of testing (indicated in test note).

i. *New requirements.* None.

ii. *Newly codified requirements.*

None.

iii. *Revisions to existing requirements.*

Part 158 currently requires residue data (153–4) for microbial pesticides, but does not lay out clearly the various underlying studies for fulfilling the actual requirement. EPA proposes the following be listed to provide greater clarity and transparency of the data that are actually required (R) to support registration: Background for residue analysis of microbial pest control agents (guideline 885.2000), chemical identity (guideline 885.2100), nature of residue (guideline 885.2200, 885.2250), analytical methods (guideline 885.2300, 885.2350), storage stability, magnitude of residue (guideline 885.2500, 885.2550, 885.2600). These data are currently required (R), therefore there is no revision in the proposed rule.

#### F. Toxicology Data Requirements

1. *General.* 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, and domestic animals, for all microbial pesticides. These data requirements include acute toxicity/ infectivity studies (oral, dermal, inhalation, pulmonary injection), a cell culture study, and hypersensitivity incidents (guideline 885.3050 through 885.3500) to be submitted. In addition, acute toxicity studies (oral, dermal, and inhalation) and the primary eye and dermal irritation studies (guidelines 870.1100 through 870.2500) are also required. The Agency wants to specially note that we are inviting public comment as to whether or not hypersensitivity incidents (guideline 885.4300) is addressed adequately via

the § 152.125, FIFRA section 6 (a)(2) data requirement, also discussed in the preamble for biochemical pesticides.

The following identifies the revisions to the current § 158.740 for microbial toxicology data requirements. Revisions include name changes, test note clarifications, revisions under which use pattern data are triggered (e.g., food use versus non-food use), and clarification of other circumstances under which data are required.

2. *Toxicology data requirements.* The Agency generally discourages a registrant from pursuing registration of a microbial pesticide that is a known human pathogen, even one reported to be an opportunistic human pathogen, because it would be difficult to support a risk assessment that would show no unreasonable risk to humans. However, in some cases, a candidate microbial pesticide may:

(a) Be very closely related to a human pathogen but lack the toxins or invasive factors responsible for that disease;

(b) Be taxonomically distinct from known human pathogens, but may have picked up a toxin or other factor that could cause mammalian disease as detected by Tier I and II studies; or,

(c) Provide significant benefits that would offset some risk that might additionally be mitigated by certain use/exposure considerations.

The Agency has encountered several cases where microbial pesticides are a member of a taxonomic group containing mammalian toxins. In these instances, data gathering beyond the codified data requirements may be required to account for potential human health risks. For most applications, this kind of testing is not needed.

Generally, toxicology data from Tier I is sufficient to address the hazards related to the human health risk assessment for pathogenicity and infectivity of microbial pesticides. The most common reason for needing Tier II or higher tests is the appearance of unexplained toxicity, unusual persistence, lethality, or adverse effects related to treatment with the microbial pesticide in the Tier I studies.

Some microbial products may be lethal to rodents at the Tier I and/or Tier II levels, where the mode of action may not be sufficiently clear to allow for specific toxin or other infectivity factors to be analyzed. Furthermore, due to the nature of some microorganisms, the possibility exists that rodents may not be a truly representative test animal for determining effects on humans of a microbial pesticide.

The Agency proposes to conditionally require (CR) Infectivity/ pathogenicity as a Tier III data requirement. This

requirement allows for the possible use of alternative test species, including primates as described in the testing guidelines.

In addition, there are ten revisions, primarily name changes to the data requirements.

i. *New requirements—Infectivity/pathogenicity.* Currently this study is not required. The Agency is proposing to conditionally require (CR) a Tier III infectivity/pathogenicity analysis (guideline 885.3000) when the microbial pesticide appears to be a mammalian pathogen that might sufficiently affect humans or nontarget mammals. While it is possible that the registrant would not want to pursue a microbial registration if such testing were triggered, the Agency believe it is appropriate to establish a Tier III toxicity study requirement to evaluate the microbial pesticides potential effects in higher animals. The Agency believes this type of data would rarely be required. However, if all criteria established in the revised test notes has been exceeded, it is appropriate to require the data.

ii. *Newly codified requirements.*

None.

iii. *Revisions to existing requirements— a. Acute oral toxicity/pathogenicity.* Currently this study is required (R) with no test notes. For clarity, the Agency is proposing a name change to the more descriptive one used in the updated guidelines (guideline 885.3050). EPA also proposes a reduction in the number of test substances required to be tested. Currently, part 158 requires both MP or EP and TGAI. The proposed rule would only require (R) the TGAI to be tested. TGAI is only required for the acute oral toxicity/pathogenicity and can be done with MP or EP to avoid the “normal” acute oral toxicity for the EP if all endpoints and dosing are confirmed. The endpoint examined in the toxicity/pathogenicity include clearance and immune functioning of the test rodent. These endpoints, once determined, are not necessary for more than the TGAI. The MP and the EP are not expected to dramatically alter the pathogenicity character of the microbe so the extra testing does not add to the safety assessment. The Agency is also proposing to add a test note, indicating the acute oral study toxicity/pathogenicity can be combined with the unit dose portion of acute oral toxicity study (guideline 870.1100) if the new protocol is designed to address the endpoints of concern.

b. *Acute pulmonary toxicity/pathogenicity.* The Agency currently requires (R) the acute inhalation study

(152–31) under Tier I. The Agency is proposing acute pulmonary toxicity/pathogenicity (guideline 885.3150) to be required in lieu of the acute inhalation study. EPA also proposes a reduction in number of test substances required to be tested, currently both MP or EP and TGAI are required. The proposed rule would only require (R) the TGAI to be tested. These endpoints, once determined, are not needed for more than the TGAI. As discussed previously, the MP and the EP are not expected to dramatically alter the pathogenicity character of the microbe so the extra testing does not add to the safety assessment.

c. *Acute injection toxicity/pathogenicity (Intravenous or Intraperitoneal)*. The Agency currently requires (R) I.V., I.C., I.P. injection study. The Agency is proposing acute injection toxicity/pathogenicity (either intraperitoneal or intravenous) to also be required (R), with the test note indicating the pathway under what conditions the intravenous or intraperitoneal would be required. Intracerebral is no longer required since it has been determined that exposure would most likely result in intravenous or intraperitoneal exposure. Under this revised data requirement, the data would not be required if the active ingredient of the pesticide product is a virus.

d. *Primary dermal irritation*. The Agency currently requires (R) this data under Tier I. The Agency is proposing to conditionally require (CR) these data as Tier I, with proposed test notes better defining the conditions when the data requirement would apply. This study would be conditionally required (CR) only if dermal irritation was indicated in the acute dermal toxicity study, since it would be evident in the results of the acute dermal toxicity study if primary dermal toxicity effects could occur.

e. *Acute inhalation toxicity*. Currently the Agency conditionally requires (CR) an acute inhalation study (151–41) in Tier II on MP or EP product when data in a Tier I acute inhalation study indicate potential adverse effects (e.g., survival, replication, infectivity, toxicity). The Agency is proposing to require (R) the acute inhalation toxicity study (guideline 870.1300) as a Tier I, limiting it to testing MP or EP, no longer requiring TGAI testing, but with a test note indicating data are required only if the product can be inhaled.

f. *Hypersensitivity study and hypersensitivity incidents*. Currently the Agency requires (R) the hypersensitivity study and conditionally requires (CR) hypersensitivity incidents. The Agency is proposing to not require (NR) the

hypersensitivity study and to require (R) hypersensitivity incident reporting data. The hypersensitivity study are currently submitted as part of product characterization on known microbial hazards such as toxins and allergens.

As indicated, the Agency proposes to revise hypersensitivity incidents from the current conditionally required (CR) to proposed required (R), even under conditions of EUP's. While these types of data are already required under § 152.125, FIFRA 6(a)(2), the status of hypersensitivity incidents reporting is unclear for microbial products that have not been registered or are under an EUP. Therefore, the Agency included a requirement for hypersensitivity incident reporting for EUP's in lieu of the hypersensitivity study. As previously indicated, EPA is inviting comment as to whether or not this study is needed, since the data must already be submitted to the Agency as 6(a)(2) data.

g. *Cell culture*. The Agency proposes to rename the currently required (R) tissue culture study for all viruses to the cell culture data requirement (guideline 885.3500), since this study is a more appropriate name for the tissue culture study and would only be required when the product's active ingredient is a virus.

h. *Reproductive fertility effects*. The Agency currently conditionally requires (CR) teratogenicity data. The Agency is proposing to conditionally require (CR) reproductive and fertility effects data (guideline 885.3650). This study replaces both guidelines 152–47 and 152–53. This is actually a replacement, since the data are basically assessing the same endpoints. The Agency is also proposing to not require these data as Tier II, but as Tier III since the triggers for this study rely on toxicity endpoints which are collected in Tier II studies, i.e., guideline 885.3600.

#### G. Nontarget Organisms and Environmental Fate Data Requirements

1. *General*. The Agency uses a tiered system of ecological effects testing to assess the potential risks of pesticides to nontarget 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, or whether the pesticide should be registered for certain use patterns at all.

Higher tiered nontarget organisms and environmental fate studies may be required when basic human health assessment 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 would be required only when the potential for adverse effects is indicated by the results of lower tier studies, or to confirm the need for mitigation measures. In some cases, the results of field studies may also give rise to the need for further testing.

2. *Nontarget organisms and environmental fate data requirements*. The proposed nontarget organisms and environmental fate data table reflects the data that are currently required to support registration of new microbials. Conditions under which data may be required are stipulated in the test notes. In addition, there are a few studies that would be replaced by more appropriate studies to measure the endpoint of concern, and other studies would be deleted. These data revisions are not expected to substantively increase the nature or burden of the existing data requirements.

i. *New requirements*. None.

ii. *Newly codified requirements*.

None.

iii. *Revisions to existing requirements*.

a. *Avian Inhalation Toxicity/Pathogenicity*. The Agency currently requires (R) an avian injection test. The Agency proposes to replace the avian injection test (154–17) with the avian inhalation test (guideline 885.4100) to provide a more appropriate endpoint to assess risks to avian species. The Agency is also proposing to conditionally require (CR) this data only when the microbial pesticide appears to have toxins that indicate potential pathogenicity. The inhalation study models a more realistic route of exposure in the wild than intraperitoneal injection.

b. *Fish life-cycle study and aquatic invertebrate range testing*. The Agency proposes to replace conditionally required (CR) aquatic embryo larvae and life cycle studies (154–28) with conditionally required (CR) fish life-cycle studies (guideline 885.4700) and definitive aquatic animal tests (154–27) with aquatic invertebrate range testing (guideline 885.4650) to provide more appropriate endpoints for assessing risks to aquatic species (fish and

invertebrates). The “fish” life cycle study is more appropriate because it identifies a particular taxonomic class to be tested as opposed to “aquatic embryo and life cycle studies” which do not identify the taxonomic class or species to be tested. “Definitive aquatic animal tests” does not say what animal group (species) is to be tested and does not say what test is to be done (“definitive” is not a test name), whereas “aquatic invertebrate range testing” is more appropriate because it specifically instructs the registrant to determine which aquatic invertebrate species are susceptible to the pesticide and which are not susceptible. In summary, the Agency is proposing to revise the titles of the data requirements in order to account for species and life cycles being tested.

c. *Simulated or actual field testing for plants (guideline 850.2500)*. The Agency currently conditionally requires (CR) nontarget plant studies (154–31) as Tier III when data in Tier II indicate there is a concern. The Agency proposes to rename the data requirement to simulated or actual field testing for plants (guideline 850.2500), which is currently conditionally required (CR) on a case-by-case basis. The test notes associated with the proposed requirement are more explicit as to when the conditions would be met. In addition, these data are proposed to be conditionally required (CR) as Tier IV.

d. *Product performance*. Currently the Agency relies on § 158.640 for product performance data requirements for biochemicals and microbial pesticides. The Agency is proposing to include product performance in the regulatory text for both biochemicals and microbial pesticides to improve transparency. Product performance verification can be important for some of the biochemical and microbial pesticides since we have seen independent reports that some do not work as well as the conventional pesticide products. It is particularly useful to have product performance data for those products that want to be considered as presenting less risk than a conventional pesticide product.

e. *Subchronic toxicity/pathogenicity*. The Agency proposes to change the name of the subchronic oral toxicity study (152–42) to correspond with the current name of the test guideline.

f. *Carcinogenicity*. The Agency proposes to change the name of the oncogenicity study to carcinogenicity study (guideline 870.4200) to correspond with the current name of the test guideline.

## IX. Peer Review

### A. National Research Council Recommendations

As discussed in Unit V.A.3, the National Academy of Sciences issued a report in 1993 entitled, “Pesticides in the Diets of Infants and Children.” The study, conducted by the National Research Council, was initiated to address the question of whether the current regulatory system adequately protected infants and children from pesticide residues in food. The Council reviewed current EPA practices and data requirements related to dietary risk assessment as well as testing modifications planned by the Agency. 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 also expressed the need to investigate the effects of pesticide exposure on immunotoxic responses in infants and children (Ref. 3).

### B. FIFRA Scientific Advisory Panel

1. *1994 SAP Review*. In 1994, EPA held a two 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. While these data requirements were presented to SAP to support conventional pesticides, the majority of changes to the data requirements presented in this notice were submitted for review as subpart M: Microbial and Biochemical Pesticides Data Requirements. These revisions were generally endorsed by the SAP (Ref. 4). A copy of the 1994 SAP final report can be found in the docket for this rulemaking (docket ID number EPA–HQ–OPP–2004–0415).

The limited issues that were addressed in 1994 Panel’s specific comments are as follows:

- *Intraperitoneal study*. The issue revolved around whether an intraperitoneal study is appropriate to use when microbial size or physical properties preclude the use of intravenous study. At that time, SAP believed the intraperitoneal study was appropriate to use when microbial size

or physical properties preclude the use of intravenous study. This option is included in the proposed rule.

- *Bird species*. The issue revolved around whether the second bird study gives significant additional information for microbial effects, i.e., are the two birds species likely to respond differently to typical biocontrol microbials. At the time, SAP suggested that it was appropriate to use only the more sensitive bird species (the quail) for data requirements. This recommendation has been included in the test note.

- *Fish species*. The issue revolved around whether the second fish study was likely to provide significant information for microbials. At the time, SAP suggested that it was appropriate to use the more sensitive fish species (trout) for data requirements. The SAP recommendation was incorporated into the test note.

Additionally, SAP encouraged the Agency to carefully evaluate the data requirements for genetically engineered microbials. The SAP believed this emerging technology was still, in many respects, an unknown entity. In the future, EPA will develop data requirements for plant-incorporated protectants.

2. *1987 SAP Review—Immunotoxicity testing of biochemical pest control agents (BPCAs) (Ref. 7)*. Proposed Guidelines for Immunotoxicity Testing of Biochemical Pest Control Agents were presented to the SAP. In particular the issues revolved around the use of a single sex of test animal in the lower tiered studies. At that time, the 1987 SAP decided that there was no scientific rationale for examining both male and female animals, though this may not apply to compounds that demonstrate estrogenic activity. In this case females may be the sex of choice since they would be more sensitive to immunotoxic effects than males by this class of compounds. A second issue raised at this meeting was the inclusion of a limit test in Tier I, in which no adverse immunological effects are observed at a single high dose, then no further testing is required. The Agency was seeking advice on the scientific criteria that would support the inclusion or exclusion of a limit test in Tier I studies. At that time, the SAP deemed it appropriate for all assays in Tier I to be included since no single test can fully evaluate all cellular or functional components of the immune system. A dose that produces a large amount of general toxicity would be of concern since the general toxicity might indirectly contribute to the immunotoxicity. Immunotoxicity data

should be cautiously evaluated in this context.

3. 1986 SAP Review—Applicator/user exposure monitoring guidelines. The Series 875, Group A, Applicator/User Exposure Monitoring Guidelines were presented to SAP in January 1986. After EPA addressed SAP comments, the guidelines were finalized. The guidelines were published by the National Technical Information Service (NTIS) in 1987 (Ref. 10).

A comprehensive listing of data requirements and the year that each specific data requirement was reviewed by SAP is available in the docket for this proposed rule (Ref. 11). Additionally, copies of documents reviewed by SAP and the final reports can be found on EPA's website at <http://www.epa.gov/scipoly/sap>.

#### X. 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. The Agency believes it has taken steps, based on current scientific knowledge and experience, to minimize testing on biochemical and microbial pesticides. With respect to these types of pesticides, the Agency has implemented a tiered testing approach, thereby potentially reducing the number of studies required for registration. 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 pesticide 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 pesticide as a screen to judge whether the pesticide 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.

The Agency plays an important role in the Federal Interagency Coordinating Committee on 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; and (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 pesticide 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 would continue to be added to the test guidelines.

#### XI. 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 (mostly conventional chemical 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 site on which it was authorized to be used.

In general, a biochemical pesticide is not expected to pose endangered species concerns because it is a naturally-occurring chemical or a synthetically-derived equivalent; has a history of exposure to humans and the environment demonstrating minimal toxicity; and has a non-toxic mode of action to the target pest(s). However, the Agency has occasionally required such data for microbial pesticides (e.g., *Metarhizium anisopliae*). The microbial pesticides typically have a limited host range and affect only certain species limiting the potential of such pesticides to pose endangered species concerns. The Agency anticipates that these data could be requested in the future in connection with other registration and reregistration actions for both biochemical and microbial pesticides if lower tier studies show potential adverse effects to nontarget organisms.

In response to a Data Call-In notice on certain conventional pesticides for data on the location of all listed species, an industry taskforce 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. Thus, the Agency is requesting comment on its utility and appropriateness.

While EPA is using the best available scientific and commercial information to assess risks to listed species, uncertainties still exist. 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 nontarget and endangered plant species exposed to herbicides.

- Toxicity data to characterize potential effects to aquatic invertebrates (i.e., 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.

## XII. Research Involving Human Subjects

This proposed rule (see proposed § 158.950) would establish data requirements for applicator/user exposure studies for biochemical pesticides proposed as insect repellents. This data requirement is consistent with § 158.500 of the proposed rule for conventional pesticides (70 FR 12275, March 11, 2005).

On January 26, 2006, the EPA Administrator signed a final rule entitled *Protections for Humans Subjects in Research* (71 FR 6138, February 6, 2006), (Ref. 23) that significantly strengthens and expands the protections for subjects of “third-

party” human research (i.e., research that is not conducted or supported by EPA) by (1) prohibiting new research involving intentional exposure of pregnant women or children that is intended for submission to EPA under the pesticide laws; (2) extending the provisions of the Federal Policy for the Protection of Human Subjects of Research (the “Common Rule”) to other human research involving intentional exposure of non-pregnant adults that is intended for submission to EPA under the pesticide laws; (3) requiring submission to EPA of protocols and related information about covered human research before it is initiated; and (4) establishing an independent Human Studies Review Board to review both proposals for new research and reports of covered human research on which EPA proposes to rely under the pesticide laws.

This rule forbids EPA to rely, in its actions under the pesticide laws, on intentional-exposure human research that either involves pregnant women or children as subjects or is otherwise considered unethical, except in narrowly defined circumstances. Some studies required under this part will also be subject to subparts K, L, and M of 40 CFR part 26—the newly promulgated final rule for the protection of human subjects of research. Subpart K extends the substantive provisions of the “Common Rule”—the ethical standard that governs research with human subjects conducted or supported by EPA and other Federal departments and agencies to third-party research that involves intentional exposure of non-pregnant adults as subjects, and that is intended for submission to EPA under the pesticide laws. Subpart K also requires submission to EPA of proposals for any covered research, at least 90 days before it is initiated, for review by EPA staff and the Human Studies Review Board. Subpart L categorically prohibits any third-party research that involves intentional exposure of pregnant women, fetuses, or children as subjects, and that is intended for submission to EPA. Subpart M specifies the range of information required to be submitted along with reports of completed research with human subjects to document the ethical conduct of the research.

## XIII. Summary of Proposed Changes

The Agency has prepared a document, entitled *Summary of the Proposed Changes* (Ref. 1), to compare the current data requirements to support the registration of biochemicals and microbials, respectively, with the revised data requirements presented in

this proposed rule. The changes include: revision in test notes, revision in guideline names, revisions in tiering the various data requirements, etc. Along with the proposed changes to the data required, the Agency also proposes to revise the definitions of biochemical pesticides and microbial pesticides and to add definitions of pheromones, arthropod pheromones, and straight chain lepidopteran pheromones.

## XIV. Summary of Options

What Options did the Agency Evaluate?

The Agency evaluated three regulatory options to revising the existing data requirements. The three options are generally characterized by estimated annual cost or regulatory burden reduction and frequency of requiring data. The options as presented are intended to reflect broad conceptual approaches, and within each broad option there are other options for requiring or reducing data requirements. In addition, whether considered broadly or more narrowly, EPA’s approach is based on the primary need for sufficient information to make the FIFRA/FFDCA findings while at the same time being mindful of opportunities to reduce burden and testing where data is not value added. Again, as noted previously, the point is to emphasize first the need to meet statutory mandates.

This section will briefly cover these three options. The specific cost differences between these three regulatory options are discussed in the executive summary of the Economic Analysis for this rulemaking (Ref. 6). Overviews of estimated annual cost or regulatory burden reduction for the proposed rulemaking as a whole may be found in Unit XVI., Regulatory Assessment.

1. *Option 1 (reduced regulatory burden, potential risk)*. This low-cost approach was designed to maximize burden reduction based upon the specific nature of biochemical and microbial pesticides. Based on the non-toxic mode of action and naturally-occurring characteristics of many of these compounds, the Agency could perform a complete risk assessment based on a minimal amount of nontarget organisms and environmental fate data. For biochemical pesticides, the Agency would not require Tier I nontarget organisms and Tier II environmental fate data. For example, under this approach, the Agency would not receive any exposure or infectivity/pathogenicity data for biochemical pesticides. For microbial pesticides, the Agency would significantly reduce the



frequency of time (up to 50 percent) that proposed Tier I nontarget organisms and Tier II environmental fate data are required. The nontarget organism tests monitor the effects of proposed pesticides on nontarget birds, wild mammals, fish, insects and plants. The environmental fate tests are used to assess the persistence of biochemicals and microbial pesticides in the environment. This option would only minimally reduce the regulatory burden as compared to the changes being proposed today (described in Option 3). The Agency does not believe the decrease in burden outweighs the loss in benefits to public health and the environment from reduced availability of data for assessing environmental hazard and risk through registration decisions. The cost savings realized in this option are only marginally lower than the savings realized in the proposed option.

2. *Option 2 (significant regulatory burden, adequate risk assessment)*. This high-cost approach was evaluated based on an Agency approach of maximizing the completeness of the database. Under this approach, the Agency would require Tier I human health and environmental data requirements 100 percent of the time. For example, under this approach, the Agency would receive all exposure and infectivity/pathogenicity data, with immunotoxicity required as Tier II and Tier III data. This approach would result in significantly higher costs to pesticide registrants and increased burden to the Agency compared to the proposed approach. Additionally, unlike Option 1 and the proposed option, EPA believes that this high-cost approach would substantially raise the cost of registering a biochemical or microbial pesticide, resulting in fewer products being registered and reducing the potential for these biopesticides (generally lower risk) to compete in the marketplace to provide alternatives to conventional pesticides (generally higher risk). The extra cost and time required to register a biochemical or microbial pesticide under this option may discourage use of these safer pesticides, resulting in more, not less environmental risk.

3. *Option 3 (proposed option)*. The proposed option provides the Agency with flexibility and is a middle ground between Option 1, representing a minimal cost but potentially significant loss of environmental hazard information, and Option 2, representing the maximum availability of information, but at significantly higher cost. The Agency would require, under certain conditions, human health and environmental data from all tiering

levels (I, II, III, IV). The frequency that data is required would be based on current scientific knowledge and conditions specific to the active ingredient and use patterns. For example, the Agency proposes to require immunotoxicity as Tier II and Tier III data, conditionally require infectivity/pathogenicity data, and conditionally require exposure data for insect repellents. The proposed option is a codification of current practice, and is a balance that provides sufficient data for Agency to complete an environmental risk assessment while ensuring the lowest feasible cost and burden to applicants and the Agency.

The Agency believes the changes proposed today best serve to protect human health and the environment and allow for a complete and accurate assessment of risks, while benefitting a large number of parties, including the regulated industry, pesticide users, the general public, other Federal, State, and foreign governments, and others who are affected by or interested in pesticide use or regulation. Additionally, the net benefit of the proposed changes is expected to include a cost savings for existing and future biochemical and microbial pesticide registrants versus the current codified requirements.

Comparing the proposed option to Option 1 (low cost option), EPA believes that the modified and newly-imposed nontarget organisms and environmental fate Tier I data requirements contained in the proposed approach are needed to ensure informed risk assessment and risk management decisions on biochemical and microbial pesticide registrations.

Comparing the proposed option to Option 2 (high cost option), EPA believes that the cost and burden of requiring the Tier I human health and environmental data for all biochemical and microbial registrations would not warrant the modest benefits of marginally valuable information. EPA believes that Option 2 would reduce the adverse externalities of pesticides and unknown risks to consumers only slightly more than the proposed approach. However, the benefits of this additional data are speculative. Based on the specific nature and scientific knowledge of biochemical and microbial pesticides, these additional data (over and above what the proposed option requires) would most likely inform registration decisions very little.

## XV. References

The Agency has established a docket for this rulemaking under docket ID number EPA-HQ-OPP-2004-0415. 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. 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 as described under **ADDRESSES**.

1. U.S. EPA, 2005. "Summary of Proposed Changes to Biochemical and Microbial Pesticide Data Requirements." FEAD/OPP/U.S. EPA, Washington, D.C.

2. U.S. EPA, 2003. "OPPTS Test Guidelines." OPP/U.S. EPA, Washington, D.C.

3. National Research Council, "Pesticides in the Diets of Infants and Children," National Academy Press, Washington, D.C., 1993. Excerpt pp. 152-156.

4. FIFRA Scientific Advisory Panel (SAP). 1994 SAP Final, November 29, 1994 FIFRA Scientific Advisory Panel Meeting, November 29-30, 1994, held in Arlington, Virginia.

5. U.S. EPA. 2005. Part II. Environmental Protection Agency. Pesticides; Data Requirements for Conventional Pesticides; Proposed Rule. (70 FR 12276, March 11, 2005).

6. U.S. EPA, 2005. "Economic Analysis of the Proposed Rule Changing Data Requirements for Biochemical and Microbial Pesticides." FEAD/OPP/U.S. EPA, Washington, D.C.

7. FIFRA Scientific Advisory Panel (SAP). "A Set of Scientific Issues Being Considered by the Agency in Connection with Proposed Revision to Subdivision M, Immunotoxicity Testing of Biochemical Pest Control Agents (BPCA's)." Review from open meeting on March 24, 1987 in Arlington, Virginia.

8. U.S. EPA, 1989. "Subdivision M of the Pesticide Testing Guidelines, Microbial and Biochemical Pest Control Agents." EFED/OPP/U.S. EPA, Washington, D.C.

9. U.S. EPA, 1982. "Pesticide Assessment Guidelines, Subdivision M, Biorational Pesticides." HED/OPP/U.S. EPA, Washington, D.C.

10. U.S. EPA, 1986. "Series 875, Group A, Applicator/user Exposure Monitoring Guidelines." Presented to the FIFRA Scientific Advisory Panel (SAP), January, 1986. OPP/U.S. EPA, Washington, D.C.

11. U.S. EPA, 2005. "Overview of Proposed Data Requirements and FIFRA SAP Review." FEAD/OPP/U.S. EPA, Washington, D.C.

12. U.S. EPA, 2005. "Analysis of Data Requirements for Biochemical and

Microbial Pesticides from 1997–2004.” FEAD/OPP/U.S. EPA, Washington, D.C.

13. U.S. EPA, 2005. “Data Requirements for Biochemical and Microbial Pesticides; Proposed Rule; Consultations.” FEAD/OPP/U.S. EPA, Washington, D.C.

14. U.S. EPA, 2005. “Comparison between Current Conventional Pesticides Data Requirements and Proposed Biochemical and Microbial Pesticide Data Requirements.” FEAD/OPP/U.S. EPA, Washington, D.C.

15. OECD [2002-a] Guidance for Registration Requirements for Pheromones and Other Semiochemicals Used for Arthropod Pest Control. OECD Series on Pesticides, Number 12. Organization for Economic Cooperation and Development. February 26, 2002.

16. U.S. EPA, 2000. “p-Menthane-3,8-diol (011550) Biopesticide Registration Eligibility Document.” BPPD/OPP/U.S. EPA, Washington, D.C. Issued May, 2000.

17. OECD [2002-b] Registration of Agricultural Pesticides, Biological Pesticides—Progress on Development of Dossier/Monograph Guidance for Microbials and Pheromones. Working Group on Pesticides. Organization for Economic Cooperation and Development. January 3, 2002.

18. U.S. EPA, 2002. “Supporting Statement for an Information Collection Request: Tolerance Petitions for Pesticides on Food/Feed Crops and New Inert Ingredients.” OMB Control No. 2070–0024, EPA ICR No. 0597. OPP/U.S. EPA, Washington, D.C.

19. U.S. EPA, 2002. “Supporting Statement for an Information Collection Request: Application for New or Amended Pesticide Registration.” OMB Control No. 2070–0060, EPA ICR No. 0277. OPP/U.S. EPA, Washington, D.C.

20. U.S. EPA, 2001. “Supporting Statement for an Information Collection Request: Data Generation for Reregistration; Phase 4 and 5 Reregistration.” OMB Control No. 2070–0107, EPA ICR No. 1504. OPP/U.S. EPA, Washington, D.C.

21. U.S. EPA, 2001. “Supporting Statement for an Information Collection Request: Data Call-Ins for the Special Review and Registration Review Programs.” OMB Control No. 2070–0057, EPA ICR No. 0057. OPP/U.S. EPA, Washington, D.C.

22. U.S. EPA, 2004. “Supporting Statement for an Information Collection Request: Plant- Incorporated Protectants; CBI Substantiation and Adverse Effects Reporting.” OMB Control No. 2070–0142, EPA ICR No. 1693, Washington, D.C.

23. U.S. EPA, 2005. Protections for Subjects in Human Research: Final

Rule. (71 FR 6138, February 6, 2006). Document ID No. OPP–2003–0132.

## **XVI. FIFRA Review Requirements**

In accordance with FIFRA section 25(a), the Agency submitted a draft of this proposed regulation to the FIFRA SAP, the USDA, the Committee on Agriculture in the House of Representatives, and the Committee on Agriculture, Nutrition, and Forestry in the United States Senate.

The FIFRA SAP waived its review of this proposal because the significant scientific issues involved have already been reviewed by the SAP and additional review isn’t necessary. USDA participated fully in the interagency review process under Executive Order 12866, during which EPA and USDA discussed the registration process of microbial pesticides and the need for a coordination process when an APHIS movement permit under 7 CFR part 340 is required by USDA. As a part of related comments, USDA suggested that the Agency consider requiring the registrants to submit a copy of the applicable APHIS permits as part of the registration application for a microbial pesticide because it would facilitate coordination and improve compliance with the applicable USDA requirements. As discussed in Unit IIX., the Agency is specifically seeking public comment on the most appropriate method to ensure APHIS permitting and EPA registrations are properly coordinated.

## **XVII. Regulatory Assessment**

### *A. Regulatory Planning and Review*

Under Executive Order 12866, entitled Regulatory Planning and Review (58 FR 51735, October 4, 1993), the Office of Management and Budget (OMB) has determined that this proposed rule is a “significant regulatory action” because the proposed revision of the existing regulation to update the data requirements may raise novel legal or policy issues arising out of legal mandates, the President’s priorities, or the principles set forth in the Executive Order. Accordingly, 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 docket for this rulemaking as required by sec. 6(a)(3)(E) of the Executive Order.

In addition, EPA has prepared an economic analysis of the potential costs, benefits, and impacts associated with this proposed action, which is contained in a document entitled Economic Analysis of the Proposed Rule Changing Data Requirements for

Biochemical and Microbial Pesticides (Ref. 6). A copy of this Economic Analysis is available in the docket for this action, and is briefly summarized here.

The economic analysis considered the incremental effects between the baseline and future biochemical and microbial pesticide registration activity based on the proposed rule and two alternatives. All costs associated with presently codified 40 CFR part 158 data requirements applicable to biochemical and microbial pesticides were considered in the baseline. Future biochemical and microbial registration activity and associated costs were calculated based on a historical examination of actual pesticide registration actions between 1997 and 2004 combined with anticipated effects of new, revised, or modified 40 CFR part 158 subparts L and M data requirements. Review of 1997 to 2004 registration activity considered the type and frequency of the various biochemical and microbial pesticide registration actions that occurred, the related applicability of the various data requirements for those actions, the type and regularity of waivers granted by EPA for certain data requirements, and information about the applicants involved in those actions. Where applicable, these trends and patterns were used to predict future registration activity. Additional effects of the proposed rule due to newly proposed, revised, or modified 40 CFR part 158 subparts L and M data requirements were estimated based on EPA experience and best judgment.

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 proposed revisions include newly codified data requirements (i.e., data requirements that are not currently in part 158, but have been, in practice, required on a case-by-case basis), changes to existing requirements (i.e., a 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, or a change in use pattern for an existing requirement), and newly imposed data requirements (i.e., data requirement have never been previously imposed).

To calculate the potential costs associated with this proposal, EPA first identified the tests necessary to generate the data required, and then gathered information on the prices that laboratories typically charge a firm to conduct these tests. The prices varied

depending on conditions specific to the substance tested. Variations can be related to differences in the assumptions about the test performed (e.g., protocol, species used), or can simply be a difference in the price charged by the laboratory. Average, high, and low cost estimates were obtained for each test where possible. EPA assumed that the data required would always need to be newly generated, but often the data are already available because the registrant generated it for its own use. In such cases, the firm would simply need to submit those data to EPA, which involves less burden than generating it.

EPA then used historical data on pesticide registration actions that occurred over an eight year period (1997–2004) to identify the entities that sought pesticide registration actions in the past (Ref. 12). 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) and use pattern (how the product will be used). To estimate the average incremental cost of a new registration, a baseline testing rate (i.e., the percentage of time a particular test was historically required under the current rule) was estimated by EPA scientists based on their past experience with biochemical and microbial pesticide registrations and their involvement in developing the new data requirements. This baseline data requirement rate was compared with the percentage of time each test was required for registrations between 1997 and 2004. EPA assumes that under the proposed rule, data requirements would be imposed at the same frequency they have been required from 1997 to 2004. Additionally, EPA scientists estimated the frequency that newly imposed data requirements would be required.

Part of the Economic Analysis included preparation of 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 XVII.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. 6).

Using the currently codified requirements as the baseline for the impact analysis, the total annual impact to the pesticide industry is estimated to be a regulatory compliance cost reduction of about \$3.04 million per year, with an estimated average cost reduction of \$60,000 per firm per year.

EPA also considered a low cost alternative and a high cost alternative to the proposed rule. The low cost alternative would waive certain data requirements for biochemical pesticides and reduce the rate at which certain data requirements are required for microbial pesticides. The estimated impact of the low cost alternative is estimated to be a regulatory compliance cost reduction approximately \$3.20 million, with an estimated average cost reduction of \$63,000 per firm per year. The high cost alternative would require certain groups of data requirements 100 percent of the time, removing the discretion of Agency scientists to decide if the data are needed for a specific registration. This alternative would result in an estimated annual cost increase over current rule requirements of approximately \$3.44 million per year, or an estimated cost increase of \$67,000 per firm.

The estimated potential costs of the proposed rule acknowledges registrant is likely to request that the Agency waive certain data requirements if the registrant believes that the data are not necessary for determining the effects of a pesticide on human health and the environment. EPA estimated the annual cost savings due to waived data requirements based on both the historical rate and type of waivers granted for the period from 1997–2004, and on an analysis of how the proposed rule is expected to modify the rate at which waivers are granted. EPA estimated that the annual cost savings due to waived data requirements based on the historic waiver rates to be approximately \$29.6 million, or \$580,000 per firm per year. At the modified waiver rates predicted under the proposed rule, EPA estimated an annual cost savings of \$23.96 million, or \$470,000 per firm per year.

Since the likely impact of the proposed rule on businesses overall is expected to be mostly beneficial, the Agency believes that the rule would have no effect on the availability of pesticides to users. On balance, the Agency believes that cost savings resulting from the proposed changes to 40 CFR part 158 subparts L and M can be realized without compromising the protection of human health and the environment.

### *B. Paperwork Reduction Act*

This proposed rule does not contain any information collection requirements that require additional approval by the Office of Management and Budget (OMB) under the Paperwork Reduction Act, 44 U.S.C. 3501 et seq. 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 contained in Title 40 of the CFR, after appearing in the preamble of the final rule, may be listed in 40 CFR part 9, 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 additional information collection and paperwork burden. The information collection requirements, i.e., the paperwork collection activities, contained in this proposal related to the new data necessary to register a pesticide product are already approved by OMB under several existing information collection requests (ICR). Specifically, the program activities which would generate a paperwork burden under this proposal are covered by the following ICRs:

The activities associated with the establishment of a tolerance are currently approved under OMB Control No. 2070–0024 (EPA ICR No. 0597) (Ref. 18);

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) (Ref. 19);

The activities associated with the generation of data for reregistration are currently approved under OMB Control

No. 2070-0107 (EPA ICR No. 1504) (Ref. 20);

The activities associated with the generation of data for special review or registration review are currently approved under OMB Control No. 2070-0057 (EPA ICR No. 0922) (Ref. 21); and

Notification of genetically modified microbial pesticides. OMB Control No. 2070-0142 (EPA ICR No. 1693) (Ref. 22).

These existing ICRs cover the paperwork activities contained in this proposal because these activities already occur as part of existing program activities. These program activities are an integral part of the Agency pesticide program and the corresponding ICRs are regularly renewed as required under the PRA, such that these OMB Control Nos. are maintained valid. The approved burden in these ICRs were increased in 1996 to accommodate the potential increased burden related to the implementation of the new safety standard imposed in 1996 by FQPA and additional burden revisions related to the proposed rule are not necessary.

Based on these existing approvals, the Agency estimates that the total 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.

Direct your comments on the Agency's need for this information, the accuracy of the provided burden estimates, and any suggested methods for minimizing respondent burden, including the use of automated collection techniques, to EPA using the docket that has been established for this proposed rule (docket ID number EPA-HQ-OPP-2004-0415) at <http://www.epa.gov/edocket/>.

The Agency will consider and address comments received on the information collection requirements contained in this proposal when it develops the final rule.

### C. Regulatory Flexibility Act

Pursuant to section 605(b) of the Regulatory Flexibility Act (RFA), 5 U.S.C. 601 et seq., after considering the potential economic impacts of today's proposed rule on small entities, 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 XVII.A., and a copy of which is available in the docket for this rulemaking. The following is a brief summary of the factual basis for this certification.

Small entities include small businesses, small organizations, and small governmental jurisdictions. For purposes of assessing the impacts of today's proposed rule on small entities, small entity is defined in accordance with the RFA as: (1) A small business as defined by the Small Business Administration's (SBA) regulations at 13 CFR 121.201; (2) a small governmental jurisdiction that is a government of a city, county, town, school district, or special district with a population of less than 50,000; and (3) a small organization that is any not-for-profit enterprise which is independently owned and operated and is not dominant in its field.

Based on the industry profile that EPA prepared using historical data as part of the Economic Analysis prepared for this rulemaking, EPA has 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 impacts 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.

EPA then used historical data to estimate the impacts of the proposed rule on these small businesses. Out of 51 firms with biochemical or microbial registration actions between 1997 to 2004, financial data for determining company size was available for 40 firms, with 23 of those firms classified as small businesses. According to the analysis, all of these small entities would have realized a reduction in costs based on the proposed rule changes compared to the current part 158 data requirements. Given these estimated impacts on small businesses, EPA concluded that the proposed revisions may benefit and would not likely have a significant adverse economic impact on a substantial number of small entities.

Nonetheless, EPA is particularly interested in receiving comment from small businesses as to the estimated cost savings, expected benefits, and overall

impacts of this proposed rule. Any comments regarding the economic impacts that this proposed regulatory action may impose on small entities should be submitted to the Agency in the manner specified in the **ADDRESSES** section.

### 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 XVII, the total annual impact to the pesticide industry is estimated to be a regulatory compliance cost reduction of about \$3.04 million per year. 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 sections 202 and 205 of UMRA.

### E. Federalism Implications

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 would 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. Because instances where a State is a registrant are extremely rare, 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. Tribal Implications

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 would 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. 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 tribal governments, EPA specifically solicits comment on this proposed rule from tribal officials.

#### G. Protection of Children

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 XVII.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 would 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 would use the data and information obtained by this proposed rule to carry out its mandate under FFDCIA to give special attention to the risks of pesticides to sensitive subpopulations, especially infants and children.

#### H. Energy Implications

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. Environmental Justice

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.

#### List of Subjects

##### 40 CFR Part 158

Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

##### 40 CFR Part 172

Confidential business information, Pesticides and pests, Reporting and recordkeeping requirements, Administrative practice and procedure, Agricultural commodities, Intergovernmental relations, Labeling.

Dated: March 1, 2006.

**Stephen L. Johnson,**

*Administrator.*

Therefore, it is proposed that 40 CFR chapter I, parts 158 and 172 be amended as follows:

#### PART 158—[AMENDED]

1. By revising the authority citation for part 158 to read as follows:

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

2. By adding § 158.3 to part 158, subpart A to read as follows:

##### § 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:

*Active ingredient* means any substance (or group of structurally similar substances, if specified by the Agency) that would prevent, destroy, repel or mitigate any pest, or that functions as a plant regulator, desiccant, defoliant, or nitrogen stabilizer, within the meaning of FIFRA section 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.

*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).

#### § 158.65 [Removed]

3. By removing § 158.65.

4. By adding subparts L and M to part 158 to read as follows:

#### Subpart L—Biochemical Pesticides

Sec.

- 158.900 Biochemical pesticides subject to subpart L.
- 158.910 Biochemical pesticides data requirements.
- 158.930 Product chemistry data requirements table.
- 158.940 Residue data requirements table.
- 158.950 Human health assessment data requirements table.
- 158.960 Nontarget organisms and environmental fate data requirements table.
- 158.970 Biochemical pesticides product performance data requirements.

#### Subpart M— Microbial Pesticides

Sec.

- 158.1000 Definition and applicability.
- 158.1010 Microbial pesticide data requirements.
- 158.1020 Product analysis data requirements table.
- 158.1030 Residue data requirements table.
- 158.1040 Toxicology data requirements table.
- 158.1050 Nontarget organisms and environmental fate data requirements table.
- 158.1060 Microbial pesticides product performance data requirements.

#### Subpart L—Biochemical Pesticides

##### § 158.900 Biochemical pesticides subject to subpart L.

(a) This subpart applies to all biochemical pesticides as defined in paragraphs (b), (c) and (d) of this section.

(b) *Definition.* A *biochemical pesticide* is a pesticide that:

(1) Is a naturally-occurring substance or structurally-similar and functionally identical to a naturally-occurring substance;

(2) Has a history of exposure to humans and the environment demonstrating minimal toxicity, or in the case of a synthetically-derived biochemical pesticides, is equivalent to a naturally-occurring substance that has such a history; and

(3) Has a non-toxic mode of action to the target pest(s).

(c) *Pheromone* is a compound produced by a living organism which, alone or in combination with other such compounds, modifies the behavior of other individuals of the same species.

(1) *Arthropod pheromone* is a pheromone produced by a member of the taxonomic phylum Arthropoda.

(2) *Lepidopteran pheromone* is an arthropod pheromone produced by a member of the insect order Lepidoptera.

(3) *Straight Chain Lepidopteran pheromone* is a lepidopteran pheromone designated by an unbranched aliphatic chain (between 9 and 18 carbons) ending in an alcohol, aldehyde, or acetate functional group and containing up to three bonds in the aliphatic backbone.

(d) *Examples.* Biochemical pesticides include, but are not limited to:

- (1) Semiochemicals (insect pheromones and kairomones),
- (2) Natural plant and insect regulators,

(3) Naturally-occurring repellents and attractants, and

(4) Enzymes

(e) *Applicability.* The Agency may review on a case-by-case basis, naturally-occurring pesticides that do not clearly meet the definition of a biochemical in an effort, to ensure, to the greatest extent possible, that only the minimum testing sufficient to make scientifically sound regulatory decisions would be conducted. The Agency will review applications for registration of naturally-occurring pesticides to determine whether to review the pesticide under this subpart L.

##### § 158.910 Biochemical pesticides data requirements.

(a) Sections 158.930 through 158.970 identify the data requirements that are required to support registration of biochemical pesticides. Variations in the test conditions are identified within the test notes. Definitions that apply to all biochemical data requirements can be found in § 158.930.

(b) Each data table includes “use patterns” under which the individual

data are required, with variations including food and nonfood uses for terrestrial and aquatic applications, greenhouse, indoor, forestry, and residential outdoor applications under certain circumstances.

(c) The categories for each data requirement are “R”, which stands for required, and “CR” which stands for conditionally required. If a bracket appears around the R or CR, the data are required for both the registration and experimental use permit requests. Generally, “R” indicates that the data are more likely required than for those data requirements with CR. However, in each case, the regulatory text preceding the data table and the test notes following the data table must be used to determine whether the data requirement must be satisfied.

(d) Each table identifies the test substance that is required to be tested to satisfy the data requirement. Test substances may include: technical grade active ingredient (TGAI), manufacturing-use product (MP), end-use product (EP), typical end-use product (TEP), residue of concern, and pure active ingredient (PAI) or (All) indicating all of the above.

Commas between the test substances (i.e., TGAI, EP) indicate that data may be required on the TGAI or EP or both depending on the conditions set forth in the test note. Data requirements which list two test substances (i.e., TGAI and EP) indicate that both are required to be tested. Data requirements that list only the manufacturing product (MP) 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. Data requirements listing the EP as the test substance apply to any EP with an ingredient in the end-use formulation other than the active ingredient that is expected to enhance the toxicity of the product.

(e) The data requirements are organized into a tier-testing system with specified additional studies at higher tiers being required if warranted by adverse effects observed in lower tier studies. The lower tier studies are a subset of those required for conventional pesticides, and the studies overall are generally selected from those required for conventional pesticides.

(f) Two sets of guideline numbers are provided for some of the environmental fate data requirements. For ease of understanding, the current guidelines will be used as an interim measure until the new guidelines (in parentheses) are finalized.

**§ 158.930 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 (e) 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) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of

the active ingredient; Residue of concern= the active ingredient and its metabolites, degradates, and impurities of toxicological concern; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

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

TABLE—BIOCHEMICAL PRODUCT CHEMISTRY DATA REQUIREMENTS

Guideline Number	Data Requirement	All Use Patterns	Test Substance to support		Test notes
			MP	EP	
<b>Product Identity and Composition</b>					
880.1100	Product identity and composition	[R]	TGAI, MP	TGAI, EP	1,2
880.1200	Description of starting materials, production and formulation process	[R]	TGAI, MP	TGAI, EP	2,3
880.1400	Discussion of formation of impurities	[R]	TGAI and MP	TGAI and MP	4
<b>Analysis and Certified Limits</b>					
830.1700	Preliminary analysis	[CR]	TGAI and MP	TGAI and MP	5,8
830.1750	Certified limits	[R]	MP	EP	6
830.1800	Enforcement analytical method	[R]	MP	EP	7
<b>Physical and Chemical Characteristics</b>					
830.6302	Color	[R]	TGAI	TGAI	8
830.6303	Physical state	[R]	TGAI	TGAI and EP	8
830.6304	Odor	[R]	TGAI	TGAI	8
830.6313	Stability to normal and elevated temperatures, metals and metal ions	[R]	TGAI	TGAI	8,17
830.6315	Flammability	[CR]	MP	EP	9
830.6317	Storage stability	[R]	MP	EP	—
830.6319	Miscibility	[CR]	MP	EP	10
830.6320	Corrosion characteristics	[R]	MP	EP	—
830.7000	pH	[CR]	TGAI and MP	TGAI and EP	8,11
830.7050	UV/Visible light absorption	[R]	TGAI	TGAI	—
830.7100	Viscosity	[CR]	MP	EP	12
830.7200	Melting point/melting range	[CR]	TGAI	TGAI	8,13
830.7220	Boiling point/boiling range	[CR]	TGAI	TGAI	8,14

TABLE—BIOCHEMICAL PRODUCT CHEMISTRY DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	All Use Patterns	Test Substance to support		Test notes
			MP	EP	
830.7300	Density/relative density/bulk density	[R]	TGAI and MP	TGAI and EP	8,18
830.7520	Particle size, fiber length, and diameter distribution	[CR]	TGAI	TGAI	8,15
830.7550 830.7560 830.7570	Partition coefficient (n-Octanol /Water)	[CR]	TGAI	TGAI	16
830.7840	Water solubility	[R]	TGAI	TGAI	8
830.7950	Vapor pressure	[R]	TGAI	TGAI	8,19

(e) *Test notes.* The following test notes are applicable to the data requirements for biochemical product chemistry and are referenced in the last column of the table in paragraph (d) of this section.

1. Data must be provided in accordance with § 158.320.

2. If the MP and EP are produced by an integrated formulation system (non-registered source), these data are also required on TGAI.

3. Data must be provided in accordance with § 158.325, § 158.330, and § 158.335.

4. Data must be provided in accordance with § 158.340.

5. Data must be provided in accordance with § 158.345. Also, required to support the registration of each manufacturing-use product (including registered TGAI) and end-use products produced by an integrated formulation system. Data on other end-use products would be required on a case-by-case basis. For pesticides in the production stage, a preliminary product analytical method and data would suffice to support an experimental use permit.

6. Data must be provided in accordance with § 158.350.

7. Data must be provided in accordance with § 158.355.

8. If the TGAI cannot be isolated, data are required on the practical equivalent of the TGAI. EP testing may also be appropriate.

9. Required if the product contains combustible liquids.

10. Required if the product is an emulsifiable liquid and is to be diluted with petroleum solvents.

11. Required if the test substance is soluble or dispersible in water.

12. Required if the product is a liquid.

13. Required when the technical chemical is a solid at room temperature.

14. Required when the technical chemical is a liquid at room temperature.

15. Required for water insoluble test substances (<10<sup>-6</sup> g/l) and fibrous test substances with diameter ≥0.1 μm.

16. Required for organic chemicals unless they dissociate in water or are partially or completely soluble in water.

17. 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.

18. True density or specific density are required for all test substances. Data on bulk density is required for MPs or EPs that are solid at room temperature.

19. Not required for salts.

#### § 158.940 Residue data requirements table.

(a) *General.* Sections 158.100 through § 158.130 describe how to use this table to determine the biochemical pesticides residue data requirements for a particular pesticide product and the substance that needs to be tested. These data requirements apply to all biochemicals, e.g., semiochemicals, natural plant and insect regulators, naturally-occurring repellents and attractants, and enzymes. 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) 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. Data are also conditionally required for aquatic nonfood use if there is direct application to water.

(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 would 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 and aquatic food use, greenhouse food use, indoor food use, and indoor residential use.

(c) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; Residue of concern= the active ingredient and its metabolites, degradates, and impurities of toxicological concern; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(d) *Table.* The following table shows the data requirements for biochemical residue for specific uses. The test notes are shown in paragraph (e) of this section.



TABLE—BIOCHEMICAL RESIDUE DATA REQUIREMENTS FOR SPECIFIC USES

Guideline Number	Data Requirement	Use patterns containing data requirements				Test Substance	Test notes
		Terrestrial	Aquatic	Greenhouse Food	Indoor Food		
		Food/Feed	Food				
Supporting Information							
860.1100	Chemical identity	[CR]	[CR]	[CR]	[CR]	TGAI	1,2,4
860.1200	Directions for use	[CR]	[CR]	[CR]	[CR]	TGAI	1,3,4
Nature of Residue							
860.1300	Nature of the residue in plants	[CR]	[CR]	[CR]	[CR]	TGAI	1,4,5,6
860.1300	Nature of the residue in livestock	[CR]	[CR]	[CR]	[CR]	TGAI	1,7,8,10
860.1340	Residue analytical method-plants Residue analytical method-livestock	CR	CR	R	[CR]	Residue of concern	4,9,10
860.1360	Multiresidue method	CR	CR	R	CR	Residue of concern	10,11
Magnitude of the Residue							
860.1400	Potable water	NR	[CR]	NR	NR	TGAI	1,12
860.1400	Fish	NR	[CR]	NR	NR	TGAI	1,13
860.1400	Irrigated crops	NR	[CR]	NR	NR	TGAI	1,14
860.1460	Food handling	NR	NR	NR	[CR]	TGAI	1,15
860.1480	Meat/milk/poultry/eggs	[CR]	[CR]	[CR]	[CR]	TGAI or plant metabolites	1,7,8,10
860.1500	Crop field trials	[CR]	[CR]	[CR]	[CR]	TGAI	1,3,4
860.1520	Processed food/feed	[CR]	[CR]	[CR]	[CR]	TGAI	1,16
860.1540	Anticipated residues	[CR]	[CR]	[CR]	[CR]	Residue of concern	1,10,17
860.1550	Proposed tolerances	[CR]	[CR]	[CR]	[CR]	Residue of concern	1,18
860.1560	Reasonable grounds in support of the petition	[CR]	[CR]	[CR]	[CR]	Residue of concern	1,10
860.1650	Submittal of analytical reference standards	[CR]	[CR]	[CR]	[CR]	TGAI	10,19

(e) *Test notes.* The following test notes are applicable to the data requirements for biochemical residue for specific uses as referenced in the last column of the table contained in paragraph (d) of this section.

1. Residue chemistry data requirements apply to biochemical pesticide products when Tier II or Tier III toxicology data are required, as specified for biochemical agents in the biochemical human health assessment data requirements, § 158.950.

2. The same chemical identity data are required for biochemical product chemistry data requirements, § 158.930 with an emphasis on impurities.

3. Required information includes crops to be treated, rate of application, number and timing of applications, preharvest intervals, and relevant restrictions.

4. Residue data for outdoor residential uses are required if home gardens are to be treated and the home garden use pattern is different from use patterns where tolerances have been established.

5. Required unless it is an arthropod pheromone applied at a rate less than or equal to 150 grams active ingredient per acre.

6. Required for indoor uses where the pesticide is applied directly to food, in order to determine metabolites and/or degradates.

7. Data on metabolism in livestock are required when residues occur on a livestock

feed or if the pesticide is to be applied directly to livestock. 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.

8. Livestock feeding studies are required whenever a pesticide residue is present in livestock feed or when direct application to livestock uses occurs.

9. A residue method suitable for enforcement of tolerances is required whenever a numeric tolerance is proposed.

10. Required for indoor uses if the indoor use could result in pesticide residues in or on food or feed.

11. Data are required to determine whether FDA/USDA multiresidue methodology would detect and identify the pesticides and any metabolites.

12. Data on residues in potable water are required whenever a pesticide is to be applied directly to water, unless it can be determined that the treated water would not be used (eventually) for drinking purposes, by man or animals.

13. Data on residues in fish are required whenever a pesticide is to be applied directly to water inhabited, or that will be inhabited, by fish that may be caught or harvested for human consumption.

14. Data on residues in irrigated crops 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.

15. Data on residues in food/feed in food handling establishments are required whenever a pesticide is to be used in food/feed handling establishments.

16. Data on the nature and level of residue in processed food/feed are required when detectable residues could concentrate on processing.

17. Anticipated residue data are required when the assumption of tolerance level residues would result in predicted exposure at an unsafe level of exposure. Data on the level or residue in food as consumed would

be used to obtain a more precise estimate of potential dietary exposure.

18. The proposed tolerance must reflect the maximum residue likely to occur in crops in meat, milk, poultry, or eggs.

19. Required when a residue analytical method is required.

**§ 158.950 Human health assessment data requirements table.**

(a) *General.* (1) Sections 158.100 through 158.130 describe how to use this table to determine the human health assessment data requirements for a particular pesticide product.

(2) The data in this section (158.950) are not required for straight chain lepidopteran pheromones when applied up to a maximum use rate of 150 grams active ingredient/acre/year.

(b) *Use patterns.* (1) Food use patterns, in general, include products classified under the following general uses: terrestrial food crop use; terrestrial feed crop use; aquatic food crop use; greenhouse food crop use.

(2) Nonfood use patterns include products classified under the general use patterns of terrestrial nonfood crop use; aquatic nonfood residential use; aquatic nonfood outdoor use; aquatic

nonfood industrial use; greenhouse nonfood crop use; forestry use; residential outdoor use; residential indoor use; indoor food use; indoor nonfood use; indoor medical use.

(c) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; Residue of concern= the active ingredient and its metabolites, degradates, and impurities of toxicological concern; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(d) *Table.* The following table shows the data requirements for biochemical human health assessment. The test notes are shown in paragraph (e) of this section.

TABLE—BIOCHEMICAL HUMAN HEALTH ASSESSMENT DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Patterns		Test substance to support		Test notes
		Food	Nonfood	MP	EP	
Tier I						
Acute Testing						
870.1100	Acute oral toxicity—rat	[R]	[R]	TGAI and MP <sub>≤</sub>	TGAI and EP	1
870.1200	Acute dermal toxicity	[R]	[R]	TGAI and MP	TGAI and EP	1,2
870.1300	Acute inhalation toxicity—rat	[R]	[R]	TGAI and MP	TGAI and EP	3
870.2400	Primary eye irritation—rabbit	[R]	[R]	TGAI and MP	TGAI and EP	2
870.2500	Primary dermal irritation	[R]	[R]	TGAI and MP	TGAI and EP	1,2
870.2600	Dermal sensitization	R	R	TGAI and MP	TGAI and EP	2,4
none	Hypersensitivity incidents	[R]	[R]	All	All	5
Subchronic Testing						
870.3100	90-day oral (one species)	[R]	CR	TGAI	TGAI	6
870.3250	90-day dermal—rat	CR	CR	TGAI	TGAI	7
870.3465	90-day inhalation—rat	CR	CR	TGAI	TGAI	8
Developmental Toxicity						

TABLE—BIOCHEMICAL HUMAN HEALTH ASSESSMENT DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Patterns		Test substance to support		Test notes
		Food	Nonfood	MP	EP	
870.3700	Prenatal developmental—rat preferably	[R]	[CR]	TGAI	TGAI	9
Mutagenicity Testing						
870.5100	Bacterial reverse mutation test	[R]	[CR]	TGAI	TGAI	10
870.5300	<i>In vitro</i> mammalian cell gene mutation test	[R]	[CR]	TGAI	TGAI	10,11
Tier II						
Mutagenicity Testing ( <i>In vivo</i> cytogenetics)						
870.5385	Mammalian bone marrow chromosomal aberration	CR	CR	TGAI	TGAI	13
870.5395	Mammalian erythrocyte micronucleus	CR	CR	TGAI	TGAI	13
Developmental Toxicity						
870.3700	Prenatal developmental	[CR]	[CR]	TGAI	TGAI	9
Special Tests						
880.3550	Immunotoxicity	CR	CR	TGAI	TGAI	12,13
Applicator/User Exposure						
875.1000	Background for application exposure monitoring test guidelines	CR	CR	TGAI	TGAI	15
875.1100	Dermal outdoor exposure	CR	CR	TGAI	TGAI	15
875.1200	Dermal indoor exposure	CR	CR	TGAI	TGAI	15
875.1300	Inhalation outdoor exposure	CR	CR	TGAI	TGAI	15
875.1400	Inhalation indoor exposure	CR	CR	TGAI	TGAI	15
875.1500	Biological monitoring	CR	CR	TGAI	TGAI	15
875.1700	Product use information	[R]	[R]	TGAI	TGAI	—
Tier III						
Chronic Testing/Special Testing						
880.3800	Immune response	CR	CR	TGAI	TGAI	14
870.3800	Reproduction and fertility effects	CR	CR	TGAI	TGAI	16
870.4100	Chronic oral—rodent and nonrodent	CR	CR	TGAI	TGAI	17
870.4200	Carcinogenicity—two species—rat and mouse preferred	CR	CR	TGAI	TGAI	18

TABLE—BIOCHEMICAL HUMAN HEALTH ASSESSMENT DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Patterns		Test substance to support		Test notes
		Food	Nonfood	MP	EP	
870.5380	Mammalian spermatogonial chromosome aberration test	CR	CR	TGAI	TGAI	19
Special Testing						
870.7200	Companion animal safety	CR	CR	Choice	Choice	20

(e) *Test notes.* The following test notes are applicable to the data requirements for biochemical human health assessment as referenced in the last column of the table in paragraph (d) of this section.

1. Required unless the test material is a gas or highly volatile (vapor pressure >104torr).

P≤2. Required unless the test material is corrosive to skin or has pH <2 or >11.5.

3. Required when the pesticide, under conditions of use, would result in respirable material (e.g., gas, volatile substance or aerosol/particulate), unless it is a straight chain lepidopteran pheromone.

4. Required if repeated contact with human skin is likely to occur under conditions of use.

5. Hypersensitivity incidents must be reported as adverse effects data.

6. Required for non-food uses that are likely to result in repeated oral exposure to humans.

7. Required to support uses involving purposeful application to the human skin or which would result in comparable prolonged human exposure to the product (e.g., insect repellents) and if any of the following criteria are met:

(i) Data from a 90-day oral study are not required.

(ii) The active ingredient is known or expected to be metabolized differently by the dermal route of exposure than by the oral route and the metabolite is of toxicological concern.

(iii) The use pattern is such that the dermal route would be the primary route of exposure.

8. Required if there is a likelihood of significant levels of repeated inhalation exposure to the pesticide as a gas, vapor, or aerosol.

9. Required if the use of the product under widespread and commonly recognized practice may reasonably be expected to result in significant exposure to female humans (e.g., occupational exposure or repeated application of insect repellents directly to the skin). Tier II data is required on a different test species from Tier I data when developmental effects are observed in the first study and information on species-to-species extrapolation is needed.

10. It is required to support nonfood uses if either (i) the use is likely to result in significant human exposure; or (ii) if the active ingredient (or its metabolites) is structurally related to a known mutagen or belongs to any chemical class of compounds containing a known mutagen. Additional mutagenicity tests that may have been performed plus a complete reference list must also be submitted. Subsequent testing may be required based on the available evidence.

11. Choice of assay using either (1) mouse lymphoma L5178Y cells, thymidine kinase (tk) gene locus, maximizing assay conditions for small colony expression or detection; (2) Chinese hamster ovary (CHO) or Chinese hamster lung fibroblast (V79) cells, hypoxanthine-guanine phosphoribosyl transferase (hprt) gene locus, accompanied by an appropriate *in vivo* test for clastogenicity; or (3) CHO cells strains AS52, xanthine-guanine phosphoribosyl transferase (xprt) gene locus.

12. Required if there are effects on hematology, clinical chemistry, lymphoid organ weights and histopathology are observed in the 90-day studies.

13. Required if results from the Tier I mutagenicity tests are positive. Allowed choice of assays, initial considerations usually given to rodent bone marrow, using either metaphase analysis (aberrations) or micronucleus assay.

14. Required if adverse effects are observed in the Tier II immunotoxicity study. The protocol for evaluating adverse effects to the immune response should be developed after evaluating the effects noted in the immunotoxicity study.

15. These data are required when any human health effects assessment data indicate that the biochemical may pose a potential hazard to the applicator/user. It is recommended that the Agency be consulted prior to study initiation to determine what studies are appropriate based on the nature of the adverse effects seen in the human health assessment data and the available exposure data. Studies performed to support registration of insect repellents may require modifications to these guidelines.

16. Required if there is evidence of: (a) endocrinological effects from the subchronic toxicity studies, (b) developmental effects in the prenatal developmental toxicity study(s), or (c) genotoxicity to mammals based on results from the mutagenicity tests. The use of a combined study that utilizes the two-

generation reproduction study in rodents (guideline 870.3800) as a basic protocol for the addition of other endpoints or functional assessments in the immature animal is encouraged.

17. Required if the potential for adverse chronic effects is indicated based on any of the following:

(i) The subchronic effect level established in the following Tier I studies: 90-day feeding toxicity study, the 90-day dermal toxicity study, or the 90-day inhalation toxicity study.

(ii) The pesticide use pattern (e.g., rate, frequency, and site of application).

(iii) The frequency and level of repeated human exposure that is expected.

18. Required if the product meets either of the following criteria:

(i) The active ingredient (or any of its metabolites, degradation products, or impurities) produce(s) in Tier I subchronic studies a morphologic effect (e.g., hyperplasia or metaplasia) in any organ that potentially could lead to neoplastic change.

(ii) Adverse cellular effects suggesting carcinogenic potential are observed in Tier II immunotoxicity and Tier III immune response study or in Tier II mammalian mutagenicity assays.

In addition, a 90-day range finding study in both rats and mice is required to determine the 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.

19. Required if results from lower tiered mutation or reproductive studies indicate there is potential for chromosomal aberration to occur.

20. 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.

#### § 158.960 Nontarget organisms and environmental fate data requirements table.

(a) *General.* (1) Sections 158.100 through 158.130 describe how to use this table to determine the terrestrial and aquatic nontarget organisms and 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. In general,

for all outdoor end-use products including turf, the following studies are required: one avian acute oral, one avian dietary, one acute freshwater fish, one acute freshwater invertebrate study, plant toxicity testing and a honeybee acute contact study.

(2) The data in this section are not required for arthropod pheromones when applied at up to a maximum use rate of 150 grams active ingredient/acre/year except when the product is expected to be available to avian species (i.e., granular formulation).

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

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 nonfood use. The remaining terrestrial uses include: forestry and residential outdoor use. Data are also required for the general use patterns of aquatic food and nonfood crop use.

(c) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required;

MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; Residue of concern= the active ingredient and its metabolites, degradates, and impurities of toxicological concern; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(d) *Table.* The following table shows the data requirements for biochemical nontarget organisms and environmental fate. The test notes are shown in paragraph (e) of this section.

TABLE—BIOCHEMICAL NONTARGET ORGANISMS AND ENVIRONMENTAL FATE DATA REQUIREMENTS

Guideline Number	Data Requirement	Use Groups containing data requirements					Test Substance	Test notes
		Terrestrial	Aquatic	Greenhouse	Forestry, residential outdoor	Indoor		
		Food/feed, nonfood	Food, nonfood	Food, nonfood		Food, nonfood		
<b>Tier I</b>								
<b>Avian Testing</b>								
850.2100	Avian acute oral toxicity	[R]	[R]	CR	[R]	CR	TGAI, EP	1,2,3,4
850.2200	Avian dietary toxicity	[R]	[R]	CR	[R]	CR	TGAI, EP	1,2,3,4
<b>Aquatic Organism Testing</b>								
850.1075	Fish acute toxicity, freshwater	[R]	[R]	CR	[R]	CR	TGAI, EP	2,3,4,5
850.1010	Aquatic invertebrate acute toxicity, freshwater	[R]	[R]	CR	[R]	CR	TGAI, EP	2,3,4,5
<b>Nontarget Plant Testing</b>								
850.4100	Terrestrial Plant Toxicity, Seedling emergence	R	R	NR	R	NR	TGAI, EP	5
850.4150	Terrestrial Plant Toxicity, Vegetative vigor	R	R	NR	R	NR	TGAI, EP	5
<b>Insect Testing</b>								
880.4350	Nontarget Insect Testing	R	R	R	R	NR	TGAI	14
<b>Tier II</b>								
<b>Environmental Fate Testing</b>								
163-1 (835.1230)	Sediment and soil adsorption/desorption for parent and degradates	CR	CR	CR	CR	NR	TGAI	6
163-1 (835.1240)	Soil column leaching	CR	CR	CR	CR	NR	TGAI	6
163-2 (835.1410)	Laboratory volatilization from soil	CR	NR	CR	CR	NR	TEP	7

TABLE—BIOCHEMICAL NONTARGET ORGANISMS AND ENVIRONMENTAL FATE DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Groups containing data requirements					Test Sub-stance	Test notes
		Terrestrial	Aquatic	Green-house	Forestry, residen-tial out-door	Indoor		
		Food/feed, nonfood	Food, nonfood	Food, nonfood		Food, nonfood		
161-1 (835.2120)	Hydrolysis	CR	CR	CR	CR	NR	TGAI	6
161-1 (835.4100)	Aerobic soil metabo-lism	CR	NR	CR	CR	NR	TGAI	6
161-2 (835.2240)	Photodegradation in water	CR	CR	CR	CR	NR	TGAI	6
161-3 (835.2410)	Photodegradation on soil	CR	NR	CR	CR	NR	TGAI	6
162-2 (835.4200)	Anerobic soil metabo-lism	CR	NR	NR	NR	NR	TGAI	6
162-4 (835.4300)	Aerobic aquatic metab-olism	CR	CR	CR	CR	NR	TGAI	6
162-3(835.4400)	Anerobic aquatic me-tabolism	CR	CR	NR	NR	NR	TGAI	6
880.4425	Dispenser -water leaching	CR	NR	CR	CR	NR	EP	8
Nontarget Plant								
850.4225	Seedling emergence	R	R	NR	R	NR	TGAI	9
850.4250	Vegetative vigor	R	R	NR	R	NR	TGAI	9
Tier III								
Aquatic Fauna Chronic, Life Cycle, and Field Studies								
850.1300 850.1400 850.1500	Freshwater fish/ inver-tebrate testing	CR	CR	NR	CR	NR	TGAI	10
850.1025 850.1035 850.1045 850.1055 850.1350 850.1400 850.1500	Marine/Estuarine fish/ invertebrate animal testing	CR	CR	NR	CR	NR	TGAI	10
850.1950	Aquatic field fish/ invertebratetesting	CR	CR	NR	CR	NR	EP	10
Terrestrial Wildlife								
850.2300	Avian Reproduction	CR	CR	NR	CR	NR	TGAI	11
850.2400	Wild mammal acute toxicity	CR	CR	NR	CR	NR	TGAI	11
850.2500	Terrestrial field testing	CR	CR	NR	CR	NR	EP	11
Beneficial Insects								
850.3040	Field testing for Polli-nators	CR	CR	NR	CR	NR	TEP	12
Nontarget Plants								

TABLE—BIOCHEMICAL NONTARGET ORGANISMS AND ENVIRONMENTAL FATE DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Use Groups containing data requirements					Test Substance	Test notes
		Terrestrial	Aquatic	Greenhouse	Forestry, residential outdoor	Indoor		
		Food/feed, nonfood	Food, nonfood	Food, nonfood		Food, nonfood		
850.4225 850.4250 850.4300 850.4450	Nontarget plant	CR	CR	NR	CR	NR	TGAI	13

(e) *Test notes.* The following test notes are applicable to the data requirements for biochemical nontarget organisms and environmental fate as referenced in the last column of the table contained in paragraph (d) of this section.

1. Required for the EP when any end-use formulation may contain other ingredients that may be toxic to nontarget organisms or to support arthropod pheromones that would be available to avian wildlife, (e.g., a granular product).

2. Tests for pesticides intended solely for indoor application would be required on a case-by-case basis, depending on use pattern, physical/chemical properties, production volume, and other pertinent factors.

3. Not required for any use groups if the pesticide is highly volatile (estimated volatility >5 X 10<sup>-5</sup> atm m<sup>3</sup>/mol).

4. Preferred test species are bobwhite quail, mallard, or redwing blackbird for avian acute oral toxicity studies; bobwhite quail or mallard for avian dietary studies, rainbow trout for acute freshwater fish studies; and *Daphnia magna* for acute freshwater invertebrate studies.

5. Required for the EP when the end-use formulation may contain other ingredients that may be toxic to nontarget organisms.

6. Required on a case-by-case basis when results from Tier I studies indicate adverse effects.

7. Required when results of any one or more of the nontarget organism studies in Tier I indicate potential adverse effects on nontarget organisms and the pesticide is to be applied on land.

8. Required when results of any one or more of the nontarget organism studies in Tier I indicate potential adverse effects on nontarget organisms and the pesticide is to be applied in a passive dispenser.

9. Required to support registration of known phytotoxicants, i.e. herbicides, desiccants, defoliant, and plant growth regulators.

10. Required if environmental fate characteristics indicate that the estimated environmental concentration of the pesticide in the aquatic environment is >0.01 of any EC<sub>50</sub> or LC<sub>50</sub> determined in the aquatic nontarget organism testing.

11. Required if either of the following criteria are met:

(i) Environmental fate characteristics indicate that the estimated concentration of the pesticide in the terrestrial environment is

>0.20 the avian dietary LC<sub>50</sub> or equal to or >0.20 the avian oral single dose LD<sub>50</sub> (converted to ppm).

(ii) The pesticide or any of its metabolites or degradation products are stable in the environment to the extent that potentially toxic amounts may persist in the avian or mammalian feed.

12. Required when results of Tier I nontarget organism studies indicate potential adverse effects on nontarget insects and results of Tier II tests indicate exposure of nontarget insects. Additional insect species may have to be tested if necessary to address issues raised by use patterns and potential exposure of important nontarget insect species, (e.g., threatened or endangered species).

13. Required if the product is expected to be transported from the site of application by air, soil, or water. The extent of movement would be determined by the results of the Tier II environmental fate studies.

14. Required depending on pesticide mode of action, method and timing of application, and results of any available efficacy data. Typically the honeybee acute toxicity guideline (guideline 850.3020) satisfies this requirement, however additional nontarget insect species may have to be tested if necessary to address issues raised by use patterns and potential exposure of important nontarget insect species, e.g., endangered species.

**§ 158.970 Biochemical pesticides product performance data requirements.**

Product performance data must be developed for all biochemical pesticides. However, the Agency typically does not require applicants to submit such efficacy data unless the pesticide product bears a claim to control public health pests, such as pest microorganisms infectious to man in any area of the inanimate environment or a claim to control vertebrates (including but not limited to: rodents, birds, bats, canids, and skunks) or invertebrates (including but not limited to: mosquitoes and ticks) that may directly or indirectly transmit diseases to humans. However, each registrant must ensure through testing that his products are efficacious when used in accordance with label directions and commonly accepted pest control practices. The Agency reserves the right

to require, on a case-by-case basis, submission of efficacy data for any pesticide product registered or proposed for registration.

**Subpart M—Microbial Pesticides**

**§ 158.1000 Definition and Applicability.**

(a) This subpart applies to all living or dead microbial pesticides as described in paragraphs (b) and (c) of this section.

(b) *Definition.* Microbial pesticide is a microorganism intended for preventing, destroying, repelling, or mitigating any pest, or intended for use as a plant regulator, defoliant, or desiccant, that:

(1) Is a eucaryotic microorganism including, but not limited to, protozoa, algae, and fungi;

(2) Is a procaryotic microorganism, including, but not limited to, bacteria; or

(3) Is an autonomous replicating microscopic element, including, but not limited to, viruses.

(c) *Applicability.* (1) In addition to the definition above, the definitions in § 158.3 also apply to this subpart.

(2) Each new isolate of a microbial pesticide is treated as a new strain and must be registered independently of any similar registered microbial pesticide strain and supported by data required in this subpart.

(3) Genetically modified microbial pesticides, may be subject to additional data or information requirements on a case-by-case basis depending on the particular microorganism and/or its parent microorganism(s), the proposed pesticide use pattern, and the manner and extent to which the organism has been genetically modified. Additional requirements may be required on a case-by-case basis.

(4) Pest control organisms such as insect predators, nematodes, and macroscopic parasites are exempt from the requirements of FIFRA as authorized by section 25(b) of FIFRA and specified in § 152.20 (a) of this chapter.

**§ 158.1010 Microbial pesticidedata requirements.**

(a) For all microbial pesticides. (1) The following § 158.1010 through 158.1050 identify the data requirements that are required to support registration of microbial pesticides. The variations in the test conditions are identified within the test notes.

(2) Each data table includes “use patterns” under which the individual data are required, with variations including all use patterns, food and nonfood uses for terrestrial and aquatic applications, greenhouse, indoor, forestry, and residential outdoor applications under certain circumstances.

(3) The categories for each data requirement are “R”, which stands for required, and “CR” which stands for conditionally required. If a bracket appears around the R or CR, the data are required for both the registration and experimental use permit requests. Generally, “R” indicates that the data are more likely required than for those data requirements with CR. However, in each case, the regulatory text preceding the data table and the test notes following the data table must be used to determine whether the data requirement must be satisfied.

(4) Each table identifies the test substance that is required to be tested to satisfy the data requirement. Test substances may include: technical grade active ingredient (TGAI),

manufacturing-use product (MP), end-use product (EP), typical end-use product (TEP), residue of concern, and pure active ingredient (PAI) or (All) indicating all of the above. Commas between the test substances (i.e., TGAI, EP) indicate that data may be required on the TGAI or EP or both depending on the conditions set forth in the test note. Data requirements which list two test substances (i.e., TGAI and EP) indicate that both are required to be tested. Data requirements that list only the manufacturing product (MP) 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. Data requirements listing the EP as the test substance apply to any EP with an ingredient in the end-use formulation other than the active ingredient that is expected to enhance the toxicity of the product.

(b) Additional data requirements for genetically modified microbial pesticides. Additional requirements for genetically modified microbial pesticides may include but are not limited to: genetic engineering techniques used; the identity of the inserted or deleted gene segment (base sequence data or enzyme restriction map of the gene); information on the control region of the gene in question; a description of the “new” traits or characteristics that are intended to be

expressed; tests to evaluate genetic stability and exchange; and selected Tier II environmental expression and toxicology tests.

**§ 158.1020 Product analysisdata requirements table.**

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the product analysis data requirements and the substance to be tested for a particular microbial pesticide. Specific conditions, qualifications, or exceptions to the designated test are identified in (d) of this section, and the test notes appear in paragraph (e) of this section.

(b) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(c) *Table.* The following table shows the data requirements for microbial product analysis. The test notes are shown in paragraph (d) of this section.

TABLE—MICROBIAL PRODUCT ANALYSIS DATA REQUIREMENTS

Guideline Number	Data Requirement	All Use patterns		Test substances to support		Test notes
		Food Use	Nonfood Use	MP	EP	
<b>Product Chemistry and Composition</b>						
885.1100	Product Identity	[R]	[R]	MP	EP	—
885.1200	Manufacturing process	[R]	[R]	TGAI and MP	TGAI and EP	1,2
	Deposition of a sample in a nationally recognized culture collection	[R]	[R]	TGAI	TGAI	—
885.1300	Discussion of formation of unintentional ingredients	[R]	[R]	TGAI and MP	TGAI and EP	2
<b>Analysis and Certified Limits</b>						
885.1400	Analysis of samples	[R]	[R]	TGAI and MP	TGAI and EP	2,3
885.1500	Certification of limits	[R]	R	MP	EP	—
<b>Physical and Chemical Characteristics</b>						
830.6302	Color	[R]	[R]	TGAI	TGAI	—



TABLE—MICROBIAL PRODUCT ANALYSIS DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	All Use patterns		Test substances to support		Test notes
		Food Use	Nonfood Use	MP	EP	
830.6303	Physical state	[R]	[R]	TGAI	TGAI	—
830.6304	Odor	[R]	[R]	TGAI	TGAI	—
830.6313	Stability to normal and elevated temperatures, metals and metal ions	[R]	[R]	TGAI	TGAI	—
830.6317	Storage stability	[R]	[R]	TGAI and MP	TGAI and EP	—
830.6319	Miscibility	[R]	[R]	MP	EP	4
830.6320	Corrosion Characteristics	[R]	[R]	MP	EP	5
830.7000	pH	[R]	[R]	TGAI	TGAI	—
830.7100	Viscosity	[R]	[R]	MP	EP	6
830.7300	Density/relative density/bulk density (specific gravity)	[R]	[R]	TGAI	TGAI	—

(d) *Test notes.* The following test notes are applicable to the data requirements for microbial product analysis as referenced in the last column of the table contained in paragraph (c) of this section.

1. If an experimental use permit is being sought, and if the pesticide is not already under full-scale production, a schematic diagram and/or description of the manufacturing process suffices.

2. If an experimental use permit is being sought, and if the product is not already under full-scale production, a discussion of unintentional ingredients is required to be submitted to the extent this information is available.

3. Required to support registration of each manufacturing-use product and end-use product. This analysis must be conducted at the point in the production process after which there would be no potential for microbial contamination or microbial regrowth. For pesticides in the production stage, a preliminary product analytical method and data would suffice to support an

experimental use permit. For full registration, generally an analysis of samples is a compilation of batches, over a period of time, depending on the frequency of manufacturing.

4. Only required for emulsifiable liquid forms of microbial pesticides.

5. Required when microbial pesticides are packaged in metal, plastic, or paper containers.

6. Only required for liquid forms of microbial pesticides.

**§ 158.1030 Residue data requirements table.**

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the residue chemistry data requirements and the substance to be tested for a particular microbial pesticide. Specific conditions, qualifications, or exceptions to the designated test appear in (d) of this

section, and the procedures appear in paragraph (e) of this section.

(b) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (d) of this section, and apply to the individual tests in the following table:

(c) *Table.* The following table shows the data requirements for microbial residue. The test notes are shown in paragraph (d) of this section.

TABLE—MICROBIAL RESIDUE DATA REQUIREMENTS

Guideline Number	Data Requirement	All Use Patterns	Test Substance Data to support MP or EP	Test notes
885.2000	Background for Residue analysis of microbial pest control agents	[CR]	EP	1
885.2100	Chemical Identity	[CR]	EP	1
885.2200	Nature of the Residue in plants	[CR]	EP	1
885.2250	Nature of the Residue in animals	[CR]	EP	1

TABLE—MICROBIAL RESIDUE DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	All Use Pat-terns	Test Sub-stance Data to support MP or EP	Test notes
885.2300	Analytical methods—plants	[CR]	TGAI	1
885.2350	Analytical methods-animals	[CR]	TGAI	1
885.2400	Storage Stability	[CR]	EP	1
885.2500	Magnitude of residue in plants	[CR]	EP	1
885.2550	Magnitude of residues in meat, milk, poultry, eggs	[CR]	EP	1
885.2600	Magnitude of residues in potable water, fish, and irrigated crops	[CR]	EP	1

(d) *Test notes.* The following test note is applicable to the data requirements for microbial residue as referenced in the last column of the table contained in paragraph (c) of this section.

1. Required when the results of testing:  
i. Indicate the potential to cause adverse human health effects or the product characterization indicates the microbial pesticide has a significant potential to produce a mammalian toxin; and ii. The use pattern is such that residues may be present in or on food or feed crops.

**§ 158.1040 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) This category includes products classified under the following general uses: terrestrial food and nonfood crop use; terrestrial feed crop use; aquatic food and nonfood crop use; greenhouse food and nonfood crop use; forestry; residential outdoor and indoor; and indoor food use.

(2) Nonfood use patterns include products classified under the general use patterns of terrestrial nonfood crop use; aquatic nonfood residential use; aquatic nonfood outdoor use; aquatic nonfood industrial use; greenhouse nonfood crop use; forestry use; residential outdoor use; residential indoor use; indoor food use; indoor nonfood use.

(c) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(d) *Table.* The following table shows the data requirements for microbial toxicology. The test notes are shown in paragraph (e) of this section.

TABLE—MICROBIAL TOXICOLOGY DATA REQUIREMENTS

Guideline Number	Data Requirement	All Use patterns	Test substance	Test notes
Tier I				
885.3050	Acute oral toxicity/pathogenicity	[R]	TGAI	1
885.3150	Acute pulmonary toxicity/pathogenicity	[R]	TGAI	—
885.3200	Acute injection toxicity/pathogenicity/(intravenous) Acute injection toxicity/pathogenicity/(intraperitoneal)	[R]	TGAI	2
885.3400	Hypersensitivity incidents	[R]	All	3
885.3500	Cell culture	[R]	TGAI	4
870.1100	Acute oral toxicity	[R]	MP , EP	1,5
870.1200	Acute dermal toxicity	[R]	MP , EP	5
870.1300	Acute inhalation toxicity	[R]	MP , EP	5,7
870.2400	Acute eye irritation	[R]	MP , EP	5
870.2500	Primary dermal irritation	[CR]	MP , EP	5,6

TABLE—MICROBIAL TOXICOLOGY DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	All Use patterns	Test substance	Test notes
Tier II				
885.3550	Acute toxicology	CR	TGAI	8
885.3600	Subchronic toxicity/pathogenicity	CR	TGAI	9
Tier III				
885.3650	Reproductive fertility effects	CR	TGAI	10,14
870.4200	Carcinogenicity	CR	TGAI	11,14
870.7800	Immunotoxicity	CR	TGAI	12,14
885.3000	Infectivity/pathogenicity analysis	CR	TGAI	13,14

(e) *Test notes.* The following test notes are applicable to the data requirements for microbial toxicology as referenced in the last column of the table contained in paragraph (d) of this section:

1. The acute oral toxicity/pathogenicity study is required to support the TGAI. However, it can be combined with the unit dose portion of the acute oral toxicity study, with an EP or MP test material to fulfill the requirement for the TGAI and the MP or EP in a single study, if the new protocol is designed to address the endpoints of concern.

2. Data not required for products whose active ingredient is a virus. For test materials whose size or consistency may prevent use of an i.v. injection, the i.p. injection procedure may be employed.

3. Hypersensitivity incidents for registered products must be reported if they occur.

4. Data must be submitted only for products whose active ingredient is a virus.

5. The 870 series studies for the MP and EP are intended to provide data on the acute toxicity of the product. Waivers for any or all of these studies may be granted when the applicant can demonstrate that the combination of inert ingredients is not likely to pose any significant human health risks. Where appropriate, the limit dose approach to testing is recommended.

6. Data are required only if dermal irritation is found after dosing in acute dermal toxicity study.

7. Required when the product consists of, or under conditions of use would result in, an inhalable material (e.g., gas, volatile substances, or aerosol particulate).

8. Data required when significant toxicity, in the absence of pathogenicity and significant infectivity, is observed in acute oral, injection, or pulmonary studies (Tier I). Route(s) of exposure correspond to routes where toxicity was observed in Tier I studies. The toxic component of the TGAI is to be tested.

9. Data required when significant infectivity and/or unusual persistence is observed in the absence of pathogenicity or

toxicity in Tier I studies. Routes of exposure (oral and/or pulmonary) correspond to routes in Tier I studies where adverse effects were noted. Data may also be required to evaluate adverse effects due to microbial contaminants or to toxic byproducts.

10. Data are required when any of the following criteria are met:

(i) Significant infectivity of the microbial pest control agent (MPCA) was observed in test animals in the Tier II subchronic study and in which no significant signs of toxicity or pathogenicity were observed.

(ii) The microbial pesticide is a virus which can persist or replicate in mammalian cell culture lines.

(iii) The microbial pesticide is not amenable to thorough taxonomic classification, and is related to organisms known to be parasitic for mammalian cells.

(iv) The microbial pesticide preparation is not well purified, and may contain contaminants which are parasitic for mammals.

11. Data may be required for products known to contain or suspected to contain carcinogenic viruses or for microbial components that are identified as having significant toxicity in Tier II testing.

12. Data may be required for products known to contain or suspected to contain viruses that can interact in an adverse manner with components of mammalian immune system.

13. An analysis of human infectivity/pathogenicity potential using scientific literature, genomic analysis, and/or actual specific cell culture/animal data may be required for products known to contain or suspected of containing intracellular parasites of mammalian cells for products that exhibit pathogenic characteristics in Tier I and/or Tier II, for products which are closely related to known human pathogens based on the Product Analysis data, or for known human pathogens that have been "disarmed" or rendered non-pathogenic for humans.

14. Test standards may have to be modified depending on the characteristics of the microorganism. Requirements may vary for

these studies depending on the active ingredient being tested. Consultation with the Agency is advised before performing these Tier III studies.

**§ 158.1050 Nontarget organisms and environmental fate data requirements table.**

(a) *General.* Sections 158.100 through 158.130 describe how to use this table to determine the terrestrial and aquatic nontarget organisms data requirements for a particular microbial 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.* Aquatic uses include: food and feed, nonfood uses (e.g., outdoor, residential, and industrial). Terrestrial uses include: Food, Feed, Non-Food, Forestry, Residential outdoor, greenhouse (food and food), Indoor (food and nonfood), and Industrial.

(c) *Key.* R=Required; [R]=Required for registrations and experimental use permits; CR=Conditionally required; [CR]=Conditionally required for registrations and experimental use permits; NR=Not required; MP=Manufacturing-use product; EP=End-use product; TEP=Typical end-use product; TGAI=Technical grade of the active ingredient; All= all of the above. Specific conditions, qualifications, or exceptions to the designated test procedures appear in paragraph (e) of this section, and apply to the individual tests in the following table:

(d) *Table.* The following table shows the data requirements for microbial nontarget organisms and environmental fate. The test notes are shown in paragraph (e) of this section.

TABLE—MICROBIAL NONTARGET ORGANISMS AND ENVIRONMENTAL FATE DATA REQUIREMENTS

Guideline Number	Data Requirement	Aquatic		Terrestrial						Test Substance	Test notes
		Food, Feed	Non-Food	Food, Feed, Non-food	For-estry	Resi-dential out-door	Green-house Food, Non-Food	Indoor Food, Non-Food	In-dustrial		
			Out door, Residential, Industrial								
Tier I											
885.4050	Avian oral toxicity	R	[R]	[R]	[R]	[R]	CR	CR	CR	TGAI	1,2
885.4100	Avian inhalation toxicity/pathogenicity	CR	CR	CR	CR	CR	CR	CR	CR	TGAI	1,2,3
885.4150	Wild mammal toxicity/pathogenicity	CR	CR	CR	CR	CR	NR	NR	CR	TGAI	1,4
885.4200	Freshwater fish toxicity/ pathogenicity	R	[R]	[R]	[R]	CR	CR	CR	CR	TGAI	1, 2,5
885.4240	Freshwater invertebrate toxicity/ pathogenicity	R	[R]	[R]	[R]	CR	CR	CR	CR	TGAI	1, 2,5
885.4280	Estuarine/Marine fish testing Estuarine and marine invertebrate testing	CR	CR	CR	CR	CR	NR	NR	CR	TGAI	1,6
885.4300	Nontarget plant testing	CR	CR	CR	[R]	CR	NR	CR	CR	TE	1,7
885.4340	Nontarget insect testing	[R]	[R]	[R]	[R]	R	CR	NR	CR	TGAI	1,8
885.4380	Honey bee testing	[R]	[[R]	[R]	[R]	R	CR	NR	CR	TGAI	1
Tier II											
885.5200	Terrestrial environmental expression tests	CR	CR	CR	CR	CR	NR	NR	CR	TGAI or TEP	9
885.5300	Freshwater environmental expression tests	CR	CR	CR	CR	CR	NR	NR	CR	TGAI or TEP	10
885.5400	Marine or estuarine environmental expression tests	CR	CR	CR	CR	CR	NR	NR	CR	TGAI or TEP	11,12
Tier III											
885.4600	Avian chronic pathogenicity and reproduction test	CR	CR	CR	CR	CR	NR	NR	CR	TGAI	12, 13
885.4650	Aquatic invertebrate range testing	CR	CR	CR	CR	CR	NR	NR	CR	TGAI	12, 14
885.4700	Fish life cycle studies	CR	CR	CR	CR	CR	NR	NR	CR	TGAI	12, 14/ ROW≤
885.4750	Aquatic ecosystem test	CR	CR	CR	CR	CR	NR	NR	CR	TGAI	15
Tier IV											

TABLE—MICROBIAL NONTARGET ORGANISMS AND ENVIRONMENTAL FATE DATA REQUIREMENTS—Continued

Guideline Number	Data Requirement	Aquatic		Terrestrial						Test Substance	Test notes
		Food, Feed	Non-Food	Food, Feed, Non-food	For-estry	Resi-dential out-door	Green-house Food, Non-Food	Indoor Food, Non-Food	In-dus-trial		
			Out door, Residential, Industrial								
850.2500 850.1950	Field testing for terrestrial wildlife and Field testing for aquatic organisms	CR	CR	CR	CR	CR	NR	NR	CR	TGAI or TEP	11, 16
850.2500	Simulated or actual field tests (birds, mammals)	CR	CR	CR	CR	CR	NR	NR	CR	TEP	16, 17, 20
850.1950	Simulated or actual field test (aquatic organisms)	CR	CR	CR	CR	CR	NR	NR	CR	TEP	16, 18, 19, 20
850.2500	Simulated or actual field tests (insect predators, parasites)	CR	CR	CR	CR	CR	NR	NR	CR	TEP	16, 18, 19, 20
850.3040	Simulated or actual field tests (insect pollinators)	CR	CR	CR	CR	CR	NR	NR	CR	TEP	16, 18, 19, 20
850.4300	Simulated or actual field tests (plants)	CR	CR	CR	CR	CR	NR	NR	CR	TEP	16, 18, 19, 20

(e) *Test notes.* The following test notes are applicable to the data requirements for microbial nontarget organism and environmental fate as referenced in the last column of the table contained in paragraph (d) of this section.

1. Tests for pesticides intended solely for indoor application would be required on a case-by-case basis, depending on use pattern, production volume, and other pertinent factors. Tests to support EUP's are based on the application timing and acreage.

2. The preferred species for the avian oral study is either the bobwhite quail or mallard duck. The preferred species for the avian inhalation toxicity/pathogenicity study and the avian chronic toxicity/pathogenicity study is the bobwhite quail. There is also the option to test the redwing black bird if there is a concern for passerine species. The rainbow trout is preferred for freshwater fish testing. However, two species (rainbow trout and bluegill sunfish are the preferred species) must be tested for uses involving direct freshwater exposure. *Daphnia magna* is the preferred species for freshwater invertebrate testing.

3. Data required when the nature of the microbial pesticide and/or its toxins indicates potential pathogenicity to birds.

4. Required on a case-by-case basis if results of tests required by § 158.1040 are inadequate or inappropriate for assessment of hazards to wild animals.

5. Required when there will be significant exposure to aquatic organisms (fish and invertebrates).

6. Required if the product is intended for direct application into the estuarine or marine environment or expected to enter this environment in significant concentrations because of expected use or mobility pattern.

7. Required if the microbial pesticide is taxonomically related to a known plant pathogen.

8. Data are not required unless an active microbial ingredient controls the target insect pest by a mechanism of infectivity; i.e. may create an epizootic condition in nontarget insects.

9. Required if toxic or pathogenic effects are observed in any of the following tests for microbial pesticides:

- (i) Avian acute oral or avian inhalation studies.
- (ii) Wild mammal studies.
- (iii) Nontarget plant studies (terrestrial).
- (iv) Honey bee studies.
- (v) Nontarget insect studies.

10. Required when toxic or pathogenic effects are observed in any of the following Tier I tests for microbial pest control agents:

- (i) Freshwater fish studies.
- (ii) Freshwater aquatic invertebrate studies.
- (iii) Nontarget plant studies (aquatic).

11. Required if product is applied on land or in fresh water or marine/estuarine environments and toxic or pathogenic effects are observed in any of the following Tier I tests for microbial pesticides:

- (i) Estuarine and marine animal toxicity and pathogenicity.
- (ii) Plant studies—estuarine or marine species.

12. An appropriate dose-response toxicity test is required when toxic effects on

nontarget terrestrial wildlife or aquatic organisms (including plants) are reported in one or more Tier I tests and results of Tier II tests indicate exposure of the microbial agent to the affected nontarget terrestrial wildlife or aquatic organisms. The protocols for these tests may have to be modified in accordance with results from the nontarget organism and environmental expression studies.

13. Required when one or more of the following are present:

(i) Pathogenic effects are observed in Tier I avian studies.

(ii) Tier II environmental expression testing indicate that long-term exposure of terrestrial animals is likely.

14. Required when product is intended for use in water or expected to be transported to water from the intended use site, and when pathogenicity or infectivity was observed in Tier I aquatic studies.

15. Required if, after an analysis of the microbial pesticide's ability to survive and multiply in the environment and what ecological habitat it would occupy, the intended use patterns, and the results of previous nontarget organisms and environmental expression tests, it is determined that use of the microbial agent may result in adverse effects on the nontarget organisms in aquatic environments. Testing is to determine if applications of the microbial pest control would be expected to disrupt the balance of populations in the target ecosystem.

16. Tier IV studies may be conducted as a condition of registration aspost-registration monitoring if the potential for unreasonable

adverse effects appears to be minimal during that period of use due to implementation of mitigation measures.

17. Required when both of the following conditions occur:

(i) Pathogenic effects at actual or expected field residue exposure levels are reported in Tier III; and

(ii) The Agency determines that quarantine methods would not prevent the microbial pesticide from contaminating areas adjacent to the test area.

18. Short term simulated or actual field studies are required when it is determined that the product is likely to cause adverse short-term or acute effects, based on consideration of available laboratory data, use patterns, and exposure rates.

19. Data from a long-term simulated field test (e.g., where reproduction and growth of confined populations are observed) and/or an actual field test (e.g., where reproduction and growth of natural populations are observed) are required if laboratory data indicate that adverse long-term, cumulative, or life-cycle effects may result from intended use.

20. Since test standards would be developed on a case-by-case basis, consultation with the Agency and development of a protocol is advised before performing these Tier IV studies.

**§ 158.1060 Microbial pesticides product performance data requirements.**

Product performance data must be developed for all microbial pesticides. However, the Agency has waived all requirements to submit efficacy data unless the pesticide product bears a claim to control public health pests, such as pest microorganisms infectious to man in any area of the inanimate environment or a claim to control vertebrates (including but not limited to: rodents, birds, bats, canids, and skunks) or invertebrates (including but not limited to: mosquitoes and ticks) that may directly or indirectly transmit diseases to humans. However, each registrant must ensure through testing that his products are efficacious when used in accordance with label directions and commonly accepted pest control practices. The Agency reserves the right to require, on a case-by-case basis, submission of efficacy data for any pesticide product registered or proposed for registration.

**PART 172—[AMENDED]**

5. The authority citation continues to read as follows:

**Authority:** 7 U.S.C. 136c, 136w. Section 172.4 is also issued under 31 U.S.C. 9701.

6. In § 172.43 revise the definition for “microbial pesticide” to read as follows:

**§ 172.43 Definitions.**

\* \* \* \* \*

*Microbial pesticide* means a microorganism intended for preventing, destroying repelling, or mitigating any pest, or intended for use as a plant regulator, defoliant, or desiccant, that:

(1) Is a eucaryotic microorganism including, but not limited to, protozoa, algae and fungi;

(2) Is a procaryotic microorganism, including, but not limited to, bacteria; or

(3) Is an autonomous replicating microscopic element, including, but not limited to, viruses.

\* \* \* \* \*

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