Pesticide Registration Manual:

Chapter 3 - Additional Considerations for Biopesticide Products

Additional Considerations for Biopesticide Products

Biopesticides are a type of pesticide derived from such natural materials as animals, plants, bacteria, and certain minerals. For example, canola oil and baking soda have pesticidal applications and are considered biopesticides. Biopesticides fall into three major classes: **microbial pesticides, plant-incorporated protectants, and biochemical pesticides**.

A separate chapter on biopesticides is included in this manual because there are different requirements for biopesticides that need to be explained in detail. This chapter should be referred to in conjunction with Chapter 2, "Registering a Pesticide Product."

Microbial pesticides are microorganisms that produce a pesticidal effect that are:

1. eukaryotic microorganisms including, but not limited to, protozoa, algae, and fungi;
2. prokaryotic microorganisms, including, but not limited to, bacteria; or
3. autonomous replicating microscopic elements, including, but not limited to, viruses.

Microbial pesticides can control many different kinds of pests, although each separate active ingredient is relatively specific for its target pest(s). For example, there are fungi that control certain weeds and other fungi that kill specific insects.

The most widely used microbial pesticides are subspecies and strains of *Bacillus thuringiensis*, or Bt. Each strain of this bacterium produces a different mix of proteins, and specifically kills one or a few related species of insect larvae. While some Bt strains control moth larvae found on plants, others are specific for larvae of flies and mosquitoes. The target insect species are determined by whether the particular Bt produces a protein that can bind to a larval gut receptor, thereby causing the insect larvae to starve.

Plant-Incorporated-Protectants (PIPs) are pesticidal substances that plants produce and the genetic material that has been added to the plant. For example, scientists can take the gene for the Bt pesticidal protein and introduce the gene into the plant's own genetic material. Then the plant, instead of the Bt bacterium, manufactures the substance that destroys the pest. EPA regulates the protein and its genetic material, but not the plant itself.

Biochemical pesticides are pesticidal substances that:

1. are naturally occurring chemicals or are synthetically derived equivalents;
2. have a history of exposure to humans and the environment demonstrating minimal toxicity, or in the case of synthetically derived biochemical pesticides, are equivalent to a naturally occurring chemical that has such a history; and
3. have a nontoxic mode of action to the target pest(s)

Biochemical pesticides include, but are not limited to:

1. semiochemicals (insect pheromones and kairomones
2. natural plant and insect regulators
3. naturally occuring repellents and attractants and
4.

Biochemical pesticides include substances, such as insect sex pheromones, which interfere with mating, as well as various scented plant extracts that attract insect pests to traps. Because it is sometimes difficult to determine whether a substance meets the criteria for classification as a biochemical pesticide, EPA has established the Biochemical Classification Committee to make such decisions. The chair of the Committee is Russell Jones.

Products Exempt from Registration

EPA has determined that pest control organisms such as insect predators, nematodes, and macroscopic parasites are exempt from the requirements of FIFRA (40 CFR 152.20(a)). In addition, pheromones and identical or substantially similar compounds labeled for use only in pheromone traps and pheromone traps in which those chemicals are the sole active ingredients are not subject to regulation under FIFRA (40 CFR 152.25(b)).

Note: The use of pheromones in traps in conjunction with conventional pesticides, or in other application methods (other than traps), is subject to regulation under FIFRA.

Minimum risk pesticides that meet certain criteria are a special class of pesticides that are not subject to federal registration requirements because their ingredients, both active and inert, are *demonstrably* safe for the intended use. They are exempt from federal registration under section 25(b) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). EPA does not review or register pesticides that satisfy the 25(b) criteria (PR Notice 2000-6), though registration is required by most states. Read more about products exempt from registration.

Registration Package for Biochemical and Microbial Pesticides

The application categories described in Chapter 2 apply to all applications for registration of conventional, biopesticide, and antimicrobial pesticide products. All applications for registration must include the data, information, forms, and fees and/or fee waiver or exemption requests as described in Chapter 2.

Biochemical and microbial pesticides are, however, subject to a different set of data requirements for registration than conventional chemicals, and are listed in Data Requirements for Registration 40 CFR Part 158:

- Subpart U: Biochemical Pesticides 158.2000
- Subpart V: Microbial Pesticides 158.2100
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EPA has published guidance for developing these data in the Biochemical Pesticides Test Guidelines, OPPTS Series 880 and the Microbial Pesticides Test Guidelines, OPPTS Series 885. Please also refer to Chapter 2 of this manual for general information on submitting an application for registration, and to Chapter 12 for additional information concerning experimental use permits.

Several helpful tips are available on the Web page for biopesticides, specifically the Biopesticide Registration Tools Web page, to aid applicants in preparing biopesticide submissions. Among these are:

1. how to avoid Confidential Statement of Formula or product chemistry issues with biopesticide submissions, and
2. examples of BPPD internal application checklists for amendment and registration application review.

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

Additional data requirements may include:

- information on the 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 characteristic that are intended to be expressed;
- tests to evaluate genetic stability and exchange; and/or
- selected Tier II environmental expression and toxicology tests.

BPPD PRIA Review Phases

The Biopesticides and Pollution Prevention Division (BPPD) has grouped its review of Pesticide Registration Improvement Extension Act (PRIA 3) actions into five phases.

- Phase I includes in–processing, specifically, documentation of receipt of the application in the Agency's tracking systems, the PRIA 21-day initial content screen (including review for consistency with PR Notice 11-3), follow up on 11-3 issues, and initiation of the PRIA 3 Preliminary Technical Screen.
- Phase II includes completion of the preliminary technical screen, any follow-up regarding deficiencies identified during the screen, and Federal Register announcements such as a notice of filing of a tolerance petition, when applicable.
- Phase III includes primary science reviews and, in some cases, drafts of a Biopesticide Regulatory Action Document (BRAD). Start dates for Phases II and III are the same, as these phases generally occur concurrently.
- Phase IV includes secondary science reviews, risk and benefit assessments, and where appropriate, preparation for a Scientific Advisory Panel (SAP) meeting.
- Phase V includes (where appropriate) SAP meeting, document development, Office of General Counsel and senior management review, sign-offs, logging the action out of the tracking system, and final Federal Register notices announcing the decision.

21-day Content Screen

When EPA receives the application and the applicable fee required by PRIA 3, the Agency will screen the application during a 21-day period to determine if it contains all required forms, labeling, and data formatted as described in the Agency's guidance (PR Notice 11-3), and documentation of fee payment. The fee payment documentation may include a request for a fee reduction or waiver or an exemption. Any deficiencies identified during the 21-day

Content Screen and uncorrected by the applicant may lead to the Agency's rejection of the application and retention of 25% of the fee.

Preliminary Technical Screen

After the 21-day Content Screen, PRIA 3 requires that a Preliminary Technical Screen be conducted within 45 days after the PRIA start date for submissions with PRIA decision review timeframes ≤6 months and within 90 days for submissions with PRIA decision review timeframes > 6 months. The purpose of the preliminary technical screen is to determine if the pesticide registration application and accompanying information and data are:

1. accurate and complete;
2. consistent with proposed labeling and any tolerance or tolerance exmption, and
3. likely to result in the granting of the application.

If the application fails the technical screen and the deficiencies cannot be corrected by the applicant within 10 business days after receipt of the Agency's notification of failure, the Agency will reject the application.

In-depth review of the data

Once the submission clears the two screens, it is placed into in-depth science review. If during this in-depth review the Agency determines that there are data deficiencies, the applicant is notified in writing of the deficiencies per 40 CFR 152.105 and allowed 75 days to make the corrections or additions to complete the application. If after 75 days, the applicant has not responded or failed to complete the application, the Agency will terminate further action and treat the application as if withdrawn. In this case, the completed application will have to be resubmitted and treated as a new application. If the applicant believes that the deficiencies cannot be corrected within 75 days, it must notify the Agency within those 75 days of the date on which it expects to complete the application. For registration applications that fall under the Pesticide Registration Improvement Act (PRIA), the Agency has timeframes in which decisions need to be made on the applications. Application deficiencies may require that the timeframe be extended, and Chapter 5's section on Negotiated Due Date Extensions describes the process for extending due dates. The Phase at which a deficiency is identified influences the new due date proposed.

Regulation of Plant-Incorporated Protectants

Consistent with the Coordinated Framework for Regulation of Biotechnology issued by the U.S. Office of Science and Technology Policy in 1986 (51 FR 23302) genetically modified (GM) crops with pesticidal traits fall under the oversight of EPA, the U.S. Department of Agriculture, and the U.S. Food and Drug Administration.

EPA's oversight focuses on the pesticidal substance produced (e.g., Bt Cry proteins) and the genetic material necessary for its production in the plant (e.g., cry genes). EPA calls this unique class of biotechnology-based pesticides plant-incorporated protectants (PIPs) and describes procedures specific for PIPs in Procedures and Requirements for Plant-Incorporated Protectants (40 CFR Part 174). Read tips regarding experimental programs for PIPs. Further guidance on small-scale field testing of PIPs and low-level presence in food is listed in PR Notice 2007-2.

Pheromone Regulatory Relief

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The Agency acknowledges that use of certain types of pheromone products presents lower risk than conventional pesticides, and also acknowledges the unique properties of these niche-type products regarding their inherently narrow host range. To promote the use of pheromone products, the Agency initiated a regulatory relief program that allows flexible confidential statements of formula for pheromone experimental use permits (EUPs) to allow for active ingredient adjustments during the course of experimentation. The Agency has also published generic tolerances and relaxed the acreage cut-off when an EUP is required. Refer to Chapter 12 on EUPs.

EPA established the following special regulations as a result of the pheromone regulatory relief program:

- exemption from requirement of a tolerance for inert materials in polymeric matrix dispensers, 40 CFR 180.1122 (58 FR 64494);
- exemption from requirement of tolerance for pheromones in polymeric matrix dispensers, 40 CFR 180.1124 (59 FR 14759);
- EUP limit raised to 250 acres for pheromones in polymeric matrix dispensers (59 FR 3681);
- EUP limit raised to 250 acres for testing of nonfood-use broadcast pheromones (59 FR 34182);
- EUP acreage limit raised to 250 acres for straight-chained pheromones (sprayables) (60 FR 168);
- tolerance exemption for straight-chained lepidopteran pheromones (sprayables), 40 CFR 180.1153 (60 FR 45399); and
- exemption from requirement of a tolerance for inert polymers in sprayable formulations, 40 CFR 180.1162 (61 FR 6551).
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Data Portion

The data portion of a registration amendment that requires product-specific data may include the following items, as applicable:

- acute toxicity data, especially if a change is proposed in the precautionary labeling or the signal word for the product, and if no previously submitted data can be cited or bridged;
- product chemistry data if the basic or alternate formulas are being changed substantially; and
- efficacy (product performance) data if proposing to add a new pest of public health significance, e.g., products to control pathogenic bacteria, viruses, mosquitoes, ticks, roaches, fleas, rats, and mice. Changes to the basic product formulation may also require additional efficacy data.

Please note that efficacy data for nonpublic-health uses must be conducted and maintained on file by the registrant, although these data are not generally required to be submitted for review.

Important Note: When submitting data, three copies are required, properly bound and formatted in accordance with PR Notice 86-5 Refer to Chapter 15 for additional information on submitting data.

Small-Scale Field Test Notifications for Certain Genetically Modified Microbial Pesticides

Notification and Reporting Requirements

Applicants must submit a notification to EPA to obtain approval before starting small-scale testing of certain genetically modified microbial pesticides or non-indigenous microbial pesticides that USDA has not previously acted upon. This approval covers intentional introduction into the environment or small-scale testing in a facility that lacks adequate containment and inactivation controls (40 CFR 172.45).

The notification should be submitted to EPA for approval at least 90 days prior to the initiation of the proposed test (40 CFR 172.46).

Mail the Notification as described in Chapter 21.

EPA will review and evaluate each Notification as quickly as possible and will make a determination no later than 90 days after receipt of the complete Notification. However, under no circumstances shall the proposed test proceed until the submitter has received notice from EPA of its approval of such test.

Before making a final determination, the Agency may

- require additional information,
- approve the proposed test provided the submitter makes certain modifications,
- require an EUP, or
- disapprove the test.

Petition for Exemption from Notification Requirements

A petition for exemption from the notification requirements for a specific microbial pesticide or class of microbial pesticides may be submitted to the Biopesticides and Pollution Prevention Division. EPA will review and evaluate petitions as expeditiously as possible (no later than 180 days after the submission or 90 days after the last submission of additional

information, whichever is later), and may request further information from the petitioner to assess the proposed exemption adequately. EPA will

- grant the petition and publish a notice of proposed rulemaking in the Federal Register for a 45-day comment period; or
- deny the petition and provide the petitioner with a written explanation of EPA's decision (40 CFR 172.52).

Substitution of an EUP Application for a Notification

In lieu of a Notification, an application for an EUP may be submitted to EPA for approval.

Contacts for Additional Information

For contact information, refer to the Organizational Charts in Chapter 21 or to the Biopesticides Contacts Web page.

References Cited in Chapter 3

Refer to Chapter 19 for information on the source of these documents.

Find Code of Federal Regulations citations in the e-CFR.

Code of Federal Regulation, Title 40

- Part 152 - Pesticide Registration and Classification Procedures
- Part 158 - Data Requirements for Registration
- Part 172 – Experimental Use Permits
- Part 174 – Procedures and Requirements for Plant-Incorporated Protectants
- Part 180 – Tolerances and Exemptions for Pesticide Chemical Residues in Food

Harmonized Test Guidelines

- Series 880 - Biochemicals Test Guidelines - Final Guidelines
- Series 885 - Microbial Pesticide Test Guidelines

Pesticide Registration Notices (PR Notices)

- PR Notice 86-5 - Standard Format for Data Submitted Under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) and Certain Provisions of the Federal Food, Drug, and Cosmetic Act (FFDCA)
- PR Notice 2007-2 - Guidance on Small-Scale Field Testing and Low-level Presence in Food of Plant-Incorporated Protectants (PIPs)
- PR Notice 2000-6 - Minimum Risk Pesticides Exempted under FIFRA Section 25(b) Clarification of Issues