Regulation of Genetically Engineered Microbial Pesticides at EPA

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Agenda

- What is a pesticidal active ingredient?
- What statutes does OPP oversee?
- Types of Regulatory Pathways
- Data Requirements
- Best Practices
What is a pesticidal active ingredient?

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

- EPA oversees microbial pesticides, both GE and non-GE. There are field testing requirements for GE microbes
Types of Microbial Active Ingredients

- Bacteriophage
- Viruses (e.g., baculoviruses, plant virus)
- Bacteria
- Fungi
- Algae
- Protozoa
- Paratransgenic insect symbionts such as *Wolbachia* in mosquitoes
EPA’s Regulatory Role

- Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) - pesticides
  - No unreasonable adverse effects upon human health and the environment
- Federal Food Drug and Cosmetic Act (FFDCA) - food and feed safety
  - Reasonable certainty of no harm from aggregate exposure to a pesticide chemical residue
- Pesticide Registration Improvement Act (PRIA)
  - Pesticide registration fee-for-services and EPA decision timelines
- Endangered Species Act
Federal Insecticide, Fungicide, Rodenticide Act (FIFRA) Actions

- Notifications for small scale field testing*
  - Genetically engineered and non-indigenous microbial pesticides, <10 acres

- Experimental Use Permits (Sec. 5)
  - Field testing on more than 10 acres of land, 1 acre of water

- Special Local Needs (Sec. 24c) and Emergency Exemptions (Sec. 18)

- Pesticide registration (Sec. 3)
  - Commercial use

- Registration review (Sec. 3(g))
  - Pesticides reassessed every 15 years

*Biotechnology notifications are a unique registration step for GE products
158 Data Requirements

• The Code of Federal Regulations (CFR) is the ‘playbook’ to FIFRA’s statutory authority

• Part 158 Subpart V describes the nature of microbial pesticides and data requirements for registration

• Primarily, genetically modified microbial pesticides require additional product characterization data
• Unlike other pesticides which require experimental use permits if field testing occurs over more than 10-acres, notification is required for small scale testing for products of biotechnology

• Unique data requirements for biotechnology notifications are in Part 172 Subpart C § 172.48

Unique field-testing requirements
• Be aware that notifications should be submitted for approval at least 90 days prior to the initiation of the proposed testing

**Unique field-testing requirements**

(5) The crops, fauna, flora, geographical description of sites, modes, dosage rates, frequency, and situation of application on or in which the pesticide is to be used.

(6) The total amount of pesticide product proposed for use in the testing.

(7) The method of application.

(8) A comparison of the natural habitat of the microbial pesticide with the proposed test site.

(9) The number of acres, structural sites, or animals/plants by State, to be treated or included in the area of experimental use.

(10) Procedures to be used to protect the test area from intrusion by unauthorized individuals.

(11) The proposed dates or periods during which the testing program is to be conducted, and the manner in which supervision of the program will be accomplished.

(12) Description of procedures for monitoring the microbial pesticide within and adjacent to the test site during the test.

(13) The method of sanitation or disposal of plants, animals, soils, farm tools, machinery etc., that will be exposed to the microbial pesticide during or after the test.

(14) Means of evaluating potential adverse effects and methods of controlling the microbial pesticide if detected beyond the test area.

(i) A statement of composition for the formulation to be tested, giving:

(1) The name and percentage by weight (or other suitable units) of each ingredient, active and inert.

(2) Production methods.

(3) Extraneous microorganisms present as contaminants.

(4) Amount and potency of any toxin present.

(5) Where applicable, the number of viable microorganisms per unit weight or volume of the product or other appropriate system for designating the quantity of active ingredient.

(m) Any additional factual information regarding the potential for unreasonable adverse effects on the environment.
Series 885 – Microbial Pesticide Test Guideline Series

Generally, the same data needs apply for GE or non-GE microbial pesticides with exceptions described in CFR Part 158 Subpart V

- Some additional data may be requested on a case-by-case basis

**Product Analysis**
- Requires information on taxonomy, natural history, target, and non-target host range
  - *For GE microbes:* Transformation event, sequence of transgene, restriction map, DNA source info, transgene stability

**Human Health**
- Introduces the AI via oral, pulmonary, and injection routes into animal surrogates

**Environmental Effects**
- Pathogenicity of related species and unrelated (wild mammals, birds, fish, beneficial insects, aquatic inverts, estuarine/marine, plants, honeybee) as well as environmental fate
- Applicants may request a waiver from data requirements or bridge from one dataset to another

**Efficacy***
- Only for public health pesticides (e.g., active against mosquitoes, termites, roaches, etc.)
Federal Food, Drug, and Cosmetic Act (FFDCA) Actions

- Tolerances and/or tolerance exemptions
  - Food and feed uses
  - Issued as rules – published in 40 CFR 180
# Pesticide Registration Improvement Act (PRIA) Timelines

<table>
<thead>
<tr>
<th>EPA Code</th>
<th>Action</th>
<th>Decision Timeline</th>
<th>FY 22’-23’ Fees</th>
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<tbody>
<tr>
<td>B590</td>
<td>New AI, tolerance exemption</td>
<td>18 months</td>
<td>$35,182</td>
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<tr>
<td>B600</td>
<td>New AI, non-food use</td>
<td>13 months</td>
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<tr>
<td>B610</td>
<td>New AI, Experimental Use Permit, with temporary tolerance or an exemption</td>
<td>10 months</td>
<td>$14,074</td>
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Biotechnology notifications are not a PRIA action and must be submitted at least 90 days prior to field testing.
What does a pesticide application look like?

- Service fee(s) required by the Pesticide Registration Improvement Act (PRIA)
- Forms describing the requested action
- The identity and quantity of all chemicals in the product
- Data on potential risks to human health and the environment, including about the potential for pesticide residues on food (if applicable)
- Proof that the product manufacturing process is reliable
- Labeling, including directions for use, contents, and appropriate warnings
Best Practices for Registration Applications

• EPA encourages **pre-submission meetings** with the Emerging Technologies Branch to discuss product concepts and data submission strategies

• Note, all small-scale field testing of pesticide products of biotechnology must be submitted to EPA as a biotechnology notification

• Submit a description of the manufacturing process for creating the end-use product that can be easily understood by the EPA reviewer as if they were an outside party following the protocol

• Fully describe how the data submitted meet the data requirements. In addition to data submitted consider including information about the lack of hazard and the lack of exposure. Cite references if possible

• If submitting literature to address a data requirement, fully describe how the publication being submitted satisfies data requirements.

• If submitting data waiver request, explain why that data requirement is inappropriate, why it is not possible to generate the data, or why the data would not be useful for the Agency's assessment.

• If 100% technical grade active ingredient (TGAI) could not used in testing, provide justification as to why

• Discuss the dose selection and its relationship to the expected environmental concentration
Regulatory Guidance


- Pesticide Registration Process, [https://www.epa.gov/pesticide-registration/about-pesticide-registration](https://www.epa.gov/pesticide-registration/about-pesticide-registration)


- Guidance for Bridging or Waiving Data Requirements, [https://www.epa.gov/pesticide-registration/bridging-or-waiving-data-requirements](https://www.epa.gov/pesticide-registration/bridging-or-waiving-data-requirements)