Pesticide Registration Manual:

Chapter 4 - Additional Considerations for Antimicrobial Products

Introduction

Antimicrobial pesticides comprise a highly diverse group of pesticides that is distinctly different from conventional pesticides and biopesticides. Although they are subject to the same basic regulatory provisions of FIFRA as are conventional pesticides and biopesticides, antimicrobial pesticides are also specifically defined in FIFRA section 2(mm) and subject to additional registration requirements described in FIFRA section 3(h). In addition, antimicrobial pesticides are managed solely by the Antimicrobials Division (AD) of the Office of Pesticide Programs. This chapter provides additional guidance unique to antimicrobial pesticides that is not covered in the other chapters.

What Is an Antimicrobial Pesticide?

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Antimicrobial pesticide” is defined in section 2(mm) of FIFRA as a pesticide that is intended to:

- disinfect, sanitize, reduce, or mitigate growth or development of microbiological organisms; or
- protect inanimate objects, industrial processes or systems, surfaces, water, or other chemical substances from contamination, fouling, or deterioration caused by bacteria, viruses, fungi, protozoa, algae, or slime; and
- is exempt from or not subject to a tolerance…or a food additive regulation.

The following products are also antimicrobial pesticides:

- any other chemical sterilant products (other than liquid chemical sterilant products exempted under FIFRA section 2(u)),
- any other disinfectant products,
- any other industrial microbiocide products, and
- any other preservative products that are not excluded below.

The following products are NOT antimicrobial pesticides:

- wood preservative or antifouling paint products for which a claim of pesticidal activity other than or in addition to antimicrobial activity is made [Note: In other words, wood preservative and antifoulant paint products that only have claims pertaining to microorganisms are antimicrobial pesticides, but the presence of additional claims such as insecticidal claims make the product a non-antimicrobial pesticide];
- agricultural fungicide products, and
- aquatic herbicide products.

The following products may qualify for exemption from FIFRA:

- treated articles exempted under 40 CFR 152.25(a).

In general, antimicrobial substances used on inanimate surfaces are subject to FIFRA, whereas antimicrobial substances used in or on living animals or humans are subject to the Federal Food, Drug, and Cosmetic Act (e.g., human or animal drugs, antiseptics, liquid chemical sterilants used on medical devices, etc.). Some antimicrobial products are subject to both FIFRA and FFDCA (i.e., dual jurisdiction products) because they involve direct or indirect food uses, or use on food contact surfaces (see Use Patterns section below for uses that may be subject to both FIFRA and FFDCA). Also refer to FDA's web site for a description of antimicrobial products that are subject to the FFDCA.

Types of Antimicrobial Pesticides

Antimicrobial pesticide products are categorized as either "public health" or "non-public health," depending on the specific claims made on each product's labeling. Registrants of public health antimicrobial pesticide products must submit efficacy data to support their application for registration or amendments to add public health claims, whereas registrants of non-public health antimicrobial pesticide products are required to generate efficacy data but not submit those data, unless EPA requests that the data be submitted on a case-by-case basis.

Public health antimicrobial pesticide products are those products that bear a claim to control pest microorganisms that pose a threat to human health, and whose presence cannot readily be observed by the user, including but not limited to, microorganisms infectious to

man in any area of the inanimate environment. A product makes a public health claim if one or more of the following apply:

1. A claim is made for control of specific microorganisms or classes of microorganisms that are directly or indirectly infectious or pathogenic to man (or both man and animals).
2. A claims is made for the pesticide product as a sterilant, disinfectant, virucide, sanitizer, or tuberculocide against microorganisms that are infectious or pathogenic to man.
3. A claim is made for the pesticide product as a fungicide against fungi infectious or pathogenic to man, or the product does not clearly state that it is intended for use only against non-public health fungi.
4. A claim is made for the pesticide product as a microbiological water purifier or microbial purification system.
5. A non-specific claim is made that the pesticide product will beneficially impact or affect public health at the site of use or in the environment in which applied, and:

- The pesticide product contains one or more ingredients that, under the criteria in 40 CFR 153.125(a), is an active ingredient with respect to a public health microorganism and there is no other functional purpose for the ingredient in the product; or
- The pesticide product is similar in composition to a registered pesticide product that makes explicit antimicrobial public health claims.

Examples of the most common public health products include:

- **Sanitizer** – A substance, or mixture of substances, that reduces the bacterial population in the inanimate environment by significant numbers, (e.g., 3 log10 reduction) or more, but does not destroy or eliminate all bacteria. Sanitizers meeting Public Health Ordinances are used on food contact surfaces and are termed sanitizing rinses.
- **Disinfectant** – A substance, or mixture of substances, that destroys or irreversibly inactivates bacteria, fungi and viruses, but not necessarily bacterial spores, in the inanimate environment. EPA registers three types of disinfectants based on the type of efficacy data submitted: Limited, General (or Broad-spectrum), and Hospital.
    - **Limited** - A disinfectant that is effective against only a specific major group of microorganisms (such as gram-positive [e.g., Staphylococcus aureus] or gram-negative [e.g., Salmonella enterica] bacteria) is considered to be a limited disinfectant.
    - **General or Broad-spectrum** – A disinfectant that is effective against both gram-positive and gram-negative bacteria (Staphylococcus aureus and Salmonella enterica) is considered to be a general or broad spectrum

disinfectant. **General or broad spectrum** disinfectants have a wide variety of uses in residential, commercial, institutional, and other sites.

- **Hospital** - A disinfectant that is a general or broad-spectrum disinfectant and also is effective against the nosocomial bacterial pathogen Pseudomonas aeruginosa is a Hospital disinfectant. These disinfectants are generally for use in hospitals, clinics, dental offices, or other health care related facilities.

- **Sterilant** – A substance, or mixture of substances, that destroys or eliminates all forms of microbial life in the inanimate environment, including all forms of vegetative bacteria, bacterial spores, fungi, fungal spores, and viruses. These products are commonly used in hospitals, laboratories, pharmaceutical clean rooms, and similar environments where sterilization is necessary.
- **Fungicide** – A substance, or mixture of substances, that destroys fungi (including yeasts) and fungal spores pathogenic to man or other animals in the inanimate environment.
- **Microbiological water purifier** – Any unit, water treatment product or system that removes, kills or inactivates all types of disease-causing microorganisms from the water, including bacteria, viruses and protozoan cysts, so as to render the treated water safe for drinking.
- **Tuberculocide** – A substance, or mixture of substances, that destroys or irreversibly inactivates tubercule bacilli in the inanimate environment.
- **Virucide –** A substance, or mixture of substances, that destroys or irreversibly inactivates viruses in the inanimate environment.

EPA's web site contains a series of Disinfectant Technical Support Section (DIS/TSS) information sheets that describe the efficacy data guidelines for public health antimicrobial pesticides. See our science policy guidance to view this information.

Nonpublic-health antimicrobial pesticide products are those products that bear a label claim to control microorganisms of economic or aesthetic significance, where the presence of the microorganism would not normally lead to infection or disease in humans. Examples of non-public health claims would include, but are not limited to, algaecides, slimicides, preservatives and products for which a pesticidal claim with respect to odor sources is made.

Find out about determining if cleaning products are considered as pesticides under FIFRA.

Animal disease pathogen and zoonotic microorganism products include products that are intended to prevent, destroy, or control microorganisms that cause significant animal diseases and/or have the potential to infect humans. Before the Foot-and-mouth disease outbreak in Great Britain in 2001, EPA generally considered these products to be non-public health products that did not require the submission of efficacy data to support label claims. However, after that event, EPA became concerned about the significant health impacts that these diseases can have on animals (or in some cases on humans) and their substantial

economic impacts. Subsequently, the Agency has been requiring that registrants submit efficacy data to support these claims. Applicants should consult the Agency for a current listing of organisms that meet these criteria (see the Organization of International Epizootics' listing).

Unique Label Claims and Efficacy Test Protocols

A registrant who wishes to add a claim for any specific public health microorganism other than those actually included in the product's basic efficacy testing (e.g, *Salmonella enterica, Staphylococcus aureus*, and *Pseudomonas aeruginosa*), must submit efficacy testing for each such additional microorganism. For example, to add a claim for the human immunodeficiency virus 1 (HIV-1) to a hospital disinfectant, the registrant must perform and submit acceptable efficacy testing supporting any claims for its product against that specific virus.

Because efficacy test protocols may not exist or be validated for certain microorganisms, the registrant should consult with EPA prior to testing with new or amended protocols. In such cases, the registrant should submit the proposed test protocol to EPA for review and acceptance prior to the study being conducted. If EPA accepts the data from the new efficacy test protocol and approves the claim requested by the registrant, then EPA will post the new protocol on its Web site for other registrants to use. For example, efficacy test protocols for several specific pathogens such as Feline Calicivirus as a surrogate for norovirus, Bovine Viral Diarrhea virus as a surrogate for Hepatitis C, and duck Hepatitis B virus as a surrogate for human Hepatitis B virus are available. (Read more about efficacy test protocols by going to the Antimicrobial Web page and using the search feature to locate a specific test or organism.)

Applying for Registration

Before assembling an application for product registration or an amendment to a product registration, an applicant or registrant should first consider contacting the appropriate Product Team and/or requesting a pre-application meeting to discuss and confirm the data and labeling requirements that apply to that application. The applicant or registrant may go to the Antimicrobial Contact List for the Product Team contacts and for guidance on requesting a pre-application meeting.

The application categories described in Chapter 2 apply to all applications for registration of conventional, biopesticide, and antimicrobial pesticide products. Also, all applications for

registration must include the data, information, forms, and fees or fee waiver requests as described in Chapter 2. However, for antimicrobial pesticide products, the following additional items may be needed as part of an application for registration:

- **Documentation of Pre-Submission Consultation**. If a pre-submission consultation has occurred, the applicant should submit written documentation describing the consultation and a copy of any Agency correspondence regarding that consultation.
- **Product Samples**. Samples of the product should NOT be submitted with an application. Product or ingredient samples may be required by the Agency for various purposes but will be requested separately.

Use Patterns

EPA's regulation "Data Requirements for Registration," which was issued in 1984 as 40 CFR Part 158, specifies the types of data and information generally required to make sound regulatory judgments under FIFRA for each pesticide proposed for experimental use, registration, amended registration, or reregistration with respect to a pesticide product's potential for causing unreasonable adverse effects. On October 26, 2007, EPA promulgated final rules establishing updated data requirements for conventional (72 FR 60934), biochemical, and microbial pesticides (72 FR 60988). On May 08, 2013 EPA promulgated the final rules (EPA-HQ-OPP-2008-0110-0111) to update the data requirements for antimicrobial pesticides. These final rules include the new Part 158W.

The use patterns in 158W, are based on similarity of use, purpose, pesticidal function and, in some cases, application practice. Applicants should consult the Agency's Antimicrobial Division Contact List to determine who to contact for questions pertaining to antimicrobial pesticide use patterns and/or for advice when a use site is not listed below.

1. **Agricultural Premises and Equipment** - This use pattern includes many indirect food uses with mostly indoor use sites:

    - farm and farm animal premises such as animal houses and pens (including milk houses), parlors, stalls, and barns;
    - transportation vehicles used to transport animals;
    - equipment such as forks, shovels, scrapers; halters, ropes, other restraining equipment; racks, mangers, feeders, waterers, troughs, and fountains; and
    - food-handling equipment such as milking equipment.

2. **Food Handling/Storage Establishments**, Premises, and Equipment - This use pattern also includes many indirect food uses due to the treatment of food contact surfaces and the resultant human exposures. All use sites are indoor and include:

    - food or feed processing plants;
    - eating establishments such as restaurants and cafeterias;
    - food storage or distribution facilities;
    - commercial transportation vehicles, shipping and storage containers;
    - food or feed stores and markets; and
    - vending machines.

3. **Commercial, Institutional and Industrial Premises, and Equipment** - This use pattern includes nonfood-contact areas of commercial sites. Typically, antimicrobial pesticides would be applied to ceilings, doors, doorknobs, fixtures, floors, light switches, stairs, walls, windows, and woodwork as part of routine cleaning practices. Included within this use pattern are school and daycare institutions. This use pattern includes both indoor and outdoor uses. Some of the uses have the potential for significant exposure due to the repetitive nature of certain exposures, and therefore may be considered as high human exposure.
4. **Residential and Public Access Premises** - This use pattern includes mostly nonfood areas, although it includes food-handling areas in homes. Some of the uses have the potential for significant exposure due to the repetitive nature of certain exposures and therefore may be considered as high human exposure. Most uses are indoor and include:
    - premises, contents, and equipment of homes, apartment, mobile homes, and shelters, including home-based daycare
    - public areas, public buildings, and public rooms; and
    - commercial kennels, or living quarters of pests, zoo animals, race horses, or laboratory animals.

5. **Medical Premises and Equipment** - Medical waste is defined as any solid waste that is generated in the diagnosis, treatment, or immunization of human beings or animals, in research pertaining thereto, or in the production of biologicals including, but not limited to, culture and stocks, pathological wastes, human blood and blood products, and sharps. This use pattern is considered to be indoor nonfood. Some of the uses have the potential for repeated exposure and therefore may be considered as high human exposure. Use sites include:
    - hospital or medical environments such as clinics, dental offices, nursing homes, sick rooms, morgues, and veterinary clinics; and
    - hospital or medical environments such as clinics, dental offices, nursing homes, sick rooms, morgues, and veterinary clinics; and
    - non-critical medical equipment such as bedpans, basins, and furniture.

6. **Human Drinking Water Systems** - Human drinking water systems include any methods used to provide potable water from raw water supplies. This use pattern is considered to be high human exposure due to the potential for human exposures via drinking water, as well as dermal exposures to the treated water. Use sites include:

    - public water systems;
    - individual water systems;
    - emergency water systems;
    - water purifier units;
    - Private water system of individual homes, farms, institutions, camp, resorts, and industrial plants; and
    - Emergency water systems for the public, campers, travelers, military, and fisherman.

EPA does not set tolerances for these uses under FIFRA.

7. **Materials Preservatives** - Materials preservatives are antimicrobial chemicals added during industrial processes to prevent the growth of microorganisms. Examples of such uses include paints, coatings, adhesives, textiles, and paper. This use pattern includes food and nonfood, and mostly indoor uses.

    This category is further divided into (a) indoor food, (b) indoor nonfood, and (c) indoor/outdoor nonfood uses. Certain uses in category (b) may have high human exposure potential, such as finger paints, and plastic making. Products registered for papermaking must have indirect food additive clearances from the U.S. Food and Drug Administration. Products registered for plastic making (i.e., where the antimicrobial in the plastic will kill microorganisms on items stored in a plastic container) require tolerances or tolerance exemptions from EPA under section 408 of FFDCA since plastics may come into contact with food items. Products in category (c) include coatings, paints (applied film), and dispersions, which have potential for widespread use.

5. **Industrial Processes and Water Systems** - Certain antimicrobial chemicals, known as microbiocides, are used to control the growth of bacteria, fungi, and algae in water systems. There are two types of systems: "once-through" and “recirculating."

- For “once-through” systems, the water is not re-used, and is therefore released into the aquatic environment or a wastewater treatment plant after a single cycle through the system. Once-through uses have the potential for significant environmental exposure when the treated water is released to the environment. Large volumes of water (as much as millions of gallons per minute) may be released directly to a river, estuary, or marine environment within minutes or hours of adding the antimicrobial to the system. In addition to the potential for environmental exposure after release, there is the potential for high human exposure via drinking water if the intake pipe for a drinking water treatment plant is downstream. Also, the water could be used in crop and/or livestock production thus providing for additional human exposure.

- However, for many uses of water in industrial plants the treated water is re-used repeatedly within the system, “recirculating” in the system multiple times until released into the aquatic environment or a wastewater treatment plant. EPA has assumed that the releases are scheduled as the antimicrobial has been “used up.” Given the lower frequency of release, resulting in lower volumes released to the environment, recirculating uses are likely to have less environmental exposure than once-through systems.

For the purposes of determining data requirements for environmental fate and ecological effects, the industrial processes and water systems use pattern are subdivided. Because of the distinct differences between the once-through and recirculating water systems, the once-through water system are grouped with the other use patterns with potential for higher environmental exposures and the recirculating water system with those use patterns with the potential for lower environmental exposures.

9. **Antifouling coatings** - Antifoulants are coatings and paints applied to boat hulls and bottoms, crab and lobster pots, and underwater structures or equipment to control the growth of freshwater or marine fouling organisms. Antifoulant coatings have the potential for high environmental exposure, most particularly for marine (both freshwater and saltwater) environments.

   Also included within this use pattern is ballast water, that is, the water that is pumped in and out of ballast tanks as a ship’s weight changes due to loading and unloading of cargo. Ballast water provides needed stability for safe operation of marine vessels. In recent years there have been significant concerns about transport of marine species from one marine environment to another in ballast water. When discharged into a new environment, the new species may become invasive and disrupt the native ecology. Ballast water treatments (such as adding an antimicrobial to the ballast water before discharge) are intended to prevent this. The Agency has reviewed few applications for

ballast water treatments, presumably because treatment of ballast water to prevent the transfer of microorganisms from one marine environment to another is relatively new. Since ballast water treatments also have the potential for high exposure to the aquatic (both freshwater and seawater) environment, EPA has grouped the ballast water treatment pesticide chemicals with the antifoulant coating pesticide chemicals.

10. **Wood Preservatives** - Wood preservative products are those that claim to control wood degradation problems due to fungal rot or decay, sapstain, molds, or wood-destroying insects. This use pattern has the potential for high exposure for both humans and the environment with mostly outdoor use sites. Certain uses can be food uses. The types of wood and the products that can be manufactured with this treated wood are:

    - freshly cut logs or lumber;
    - seasoned building materials;
    - utility poles, fence posts, and rails,
    - structural members;
    - structures and dwellings;
    - transportation vehicles (truck beds and support structures);
    - crop containers;
    - lawn furniture and decks;
    - playground equipment;
    - garden/landscape timbers; and
    - log homes.

    While wood preservative treatment plant sites are regulated under the Resource Conservation and Recovery Act (RCRA), the focus of environmental risk assessment under FIFRA is on the use of the treated wood. Exposure concerns for wood treatment products are many and varied. The nature and extent of these concerns depend primarily upon the types of wood items treated and their end-use locations. For example, pressure-treated wood may be intended specifically for use in salt or fresh water, for ground or soil contact, or for above-ground use. Sapstain-control products are for temporary treatment and are not intended for ground, soil, or aquatic contact.

11. **Swimming Pools** - Products in this use pattern are used to prevent/control the growth of bacteria or algae in the water systems of swimming pools, Jacuzzis and hot tubs. This use pattern is considered to be high human exposure. Under routine use little or no environmental exposure is expected, as the water in swimming pools, Jacuzzis, or hot tubs is considered to be separated from the natural environment. However, when draining is needed, depending on the volume of water and the location of the pool or hot tub, it is most likely that discharge would be down-the-drain to a wastewater treatment plant, to a storm drain that discharges to a stream, or directly to soil.

12. **Aquatic Areas** - Products in this use pattern are designed to control or kill slime-forming bacteria, fungi, or algae in lakes, ponds, streams, drainage ditches, and other bodies of water. In addition to the potential for environmental exposure, there is the potential for high human exposure via drinking water if the intake pipe for a drinking water treatment plant is in a lake or downstream, or through recreational activities such as swimming. Also, the water could be used in crop and/or livestock production thus providing for additional human exposure.

Other Relevant Guidance Documents

EPA's Web page for antimicrobial pesticides provides numerous guidance documents that address a wide range of science and policy issues. For example, EPA has issued many Pesticide Registration (PR) Notices since the 1970s that include guidance relevant to antimicrobials. Applicants and registrants should review these and other guidance documents available on the EPA Antimicrobials Web page before submitting an application for registration or amendment.

Contacts for Additional Information

For contact information, refer to the organizational charts in Chapter 21 or the Antimicrobials Web page.

References Cited in Chapter 4

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

Code of Federal Regulation, Title 40

- Part 152 – Pesticide registration and classification procedures
- Part 158 – Data requirements for pesticides

Federal Insecticide, Fungicide, and Rodenticide Act, as amended by the Food Quality Protection Act of August 3, 1996

- Section 2(mm)
- Section 2(u)

Federal Food, Drug and Cosmetic Act

- Section 408 - Tolerances and Exemptions for Pesticide Chemical Residues

Resource Conservation and Recovery Act (RCRA)

Label Review Manual

40 CFR Part 158W Data Requirements for Antimicrobial Pesticides