Understanding the Process for Approving Antimicrobial Pesticides

Bacteria and Viruses are Pests, Oh My!

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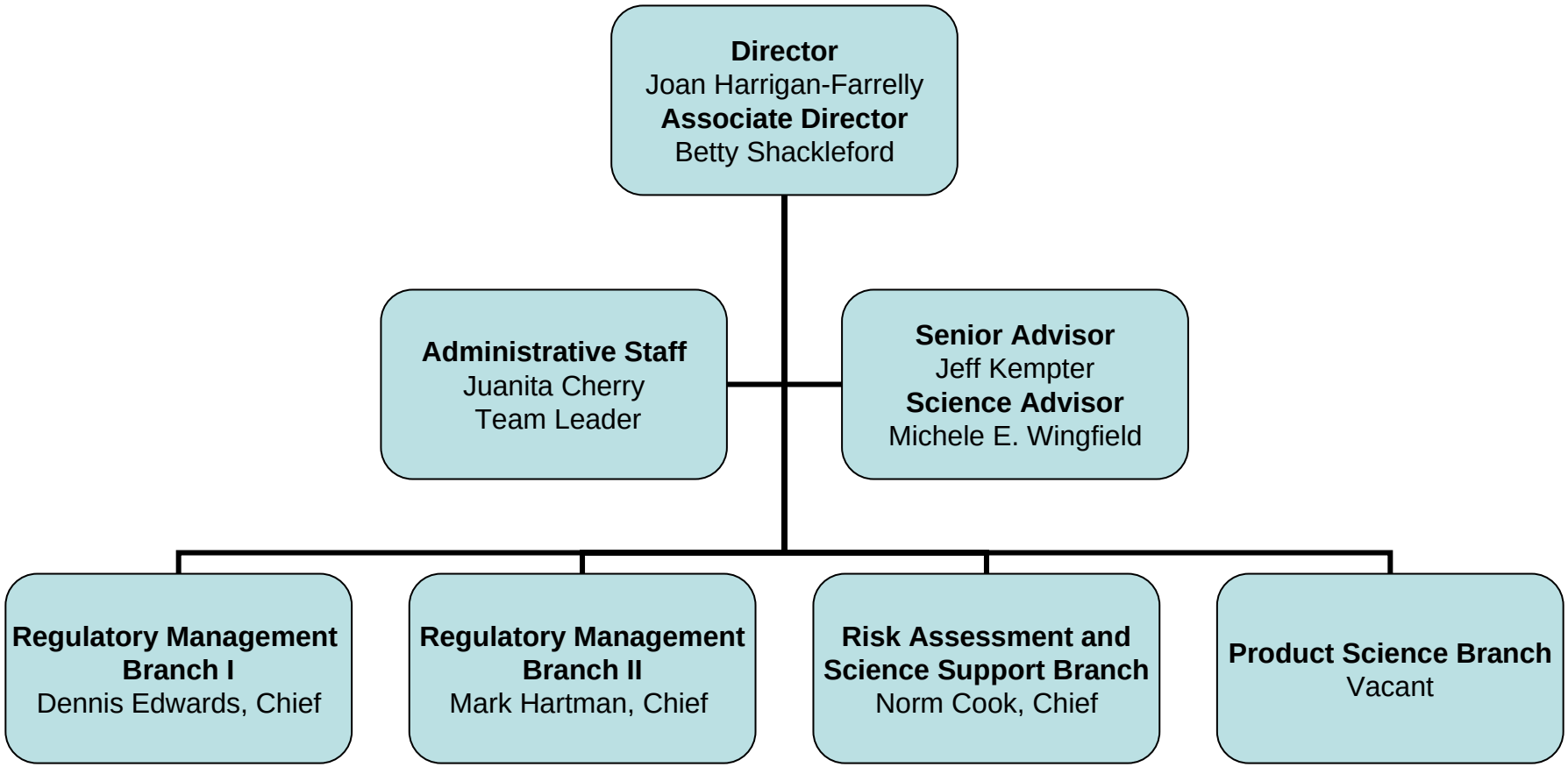
GOALS

This presentation will give attendees an understanding of the following:

- Structure of the Antimicrobials Division.
- Antimicrobial pests and pesticides.
- Product specific data requirements.
- Key components of a hospital disinfectant label.
- Addressing *Clostridium difficile*.
- Antimicrobial products effective against 2009-H1N1 flu.
- Antimicrobial Testing Program.
- Future direction of the Antimicrobials Program

The Antimicrobials Division

EPA Antimicrobials Division Organizational Structure



The Antimicrobials Division Vision

- The OPP Antimicrobials Division will ensure the protection of human health and the environment as it uses the best science and regulatory efficiencies in its registration and re-revaluation of chemicals used as pesticides against microbial pests.

Joan's Creed

Reach for the Stars!

" The greater danger for most of us lies not in setting our aim too high and falling short, but in setting our aim too low, and achieving our mark."

-Michelangelo Buonarrot-

Applicable Regulations

- Federal Insecticide, Fungicide and Rodenticide Act (FIFRA)
- Food Quality Protection Act (FQPA)
- Pesticide Regulation Improvement Act (PRIA)

EPA vs FDA Jurisdiction

- Antimicrobial products used on non-critical medical devices (items that come into contact with intact skin) and medical equipment surfaces are pesticides and subject to EPA registration.

- Antimicrobial products used on critical or semi-critical devices (items that come into contact with sterile or mucosal areas of the body) are regulated by FDA as devices (e.g., liquid chemical sterilants).
- All antimicrobials used in or on humans & animals – such as drugs, cosmetics, hand soaps.

Antimicrobial Pests and Pesticides

What is an antimicrobial pesticide?

It's 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
- Slime

Types of Antimicrobial Pesticides

The Antimicrobials Division is responsible for broad range of product types:

- Sterilants, Disinfectants, and Sanitizers: used in hospitals, nursing homes, drinking water treatment facilities, private homes, swimming pools. AD has the responsibility to ensure the efficacy of products used in hospitals and other settings to reduce or eliminate public health pathogens such as *MRSA*, *C. difficile* and Avian Influenza.
- Sanitizing Rinses: for food contact surfaces in restaurants and other food preparation areas.
- Homeland Security -- assess the effectiveness of decontamination products that can be used against chemical or biological threats such as anthrax.
- Industrial Processing Fluids: used in industrial settings like paper mills, manufacturing facilities, electrical generating plants, and oil refineries
- Antifoulants: used for Paints, coatings, adhesives
- Wood Preservatives: ensure human and ecological protection and ensure chemicals such as arsenic and chrome are not used in inappropriate settings such as playgrounds

Antimicrobial Pesticides

- **>250 active ingredients**
  - **Chlorine compounds**
    - **Sodium hypochlorite**
  - **Phenolic compounds**
  - **Peroxy compounds**
  - **Quaternary ammonium compounds**
  - **Bacteriaphages (Listeria)**

- **>5,000 products**
  - **~ 60-65% are public health products**

Public Health vs Non-Public Health Claims

- **Public Health Claims**
  - Products bearing claims to control organisms that may pose a threat to human health, either directly or through transmission of disease-causing organisms on environmental surfaces or the environment, are considered public health related antimicrobials.
- **Non-public Health Claims**
  - Products expressly claiming control of microorganisms of economic or aesthetic significance are not considered to be human health-related.

Public Health Products

- Sterilants
- Sporicides
- Disinfectants
- Non-Food Contact Surface Sanitizers
- Food Contact Surface Sanitizers
- Products Possessing Residual Self Sanitizing Activity
- Laundry Sanitizers
- Carpet Sanitizers
- Air Sanitizers
- Swimming Pool Disinfectants

Public Health Products
continued

- Other Types of Public health products
  - Anti-viral tissues
  - Copper alloy products
  - Mold products
  - Fruit and Vegetable rinses

Products that make public health related label claims require the submission of product performance data!

Registering Antimicrobial Pesticides

Process for Registering Antimicrobial Pesticides

- Applicants (Registrants) consult their Product Manager (PM) for guidance on registering their product.
- If the product contains a new active ingredient, “generic” data is submitted to RASSB for review and approval. Once approved the active ingredient is registered as a pesticide.
- Following approval of a new active ingredient, the end use formulation is registered.
- Applicants submit an application package with their product-specific data, Confidential Statement of Formula (CSF) and proposed label to their PM team.
- PM team submits data to PSB for review.
- PSB provides a Data Evaluation Report to the PM team with recommendations on the acceptability of the data.
- If data and label are acceptable, the product receives EPA registration.

Product Specific Studies

- **Acute Toxicity**
  - Known as the “6-Pack”
  - Acute oral; Acute dermal; Acute inhalation; Eye irritation; Skin irritation; Skin sensitization
  - Used to determine precautionary labeling and first aid statements

- **Product Chemistry**
  - Group A – Product Identity, Composition, and Analysis
  - Group B – Physical/Chemical Properties
  - Confidential Statement of Formula

Product Specific Studies

Product Performance (Efficacy)

- Laboratory studies submitted by the registrants to demonstrate that their product will perform against target pests (microorganisms) when the product is used according to label directions.
- Studies are conducted using standardized tests, usually from the AOAC International.

Product Performance (Efficacy) - continued

- Hospital Disinfectants must demonstrate effectiveness against *Staphylococcus aureus*, *Salmonella enterica*, and *Pseudomonas aeruginosa*, using the AOAC Use-dilution Test, Germicidal Spray Products Test, or EPA Towelette Test.
- Contact time is usually 10 minutes, although many products have demonstrated effectiveness in less than 10 minutes.

Product Performance (Efficacy) - continued

- Hospital disinfectant testing is conducted on three batches of the product, one of which is at least 60 days old. Each target microorganism is used to contaminate 60 carriers. Carriers are placed into the disinfectant for the label specified contact time.
- Contact time is usually 10 minutes, although many products have demonstrated effectiveness in less than 10 minutes.
- For a disinfectant to be considered a successful treatment, there can be no more than one positive carrier out of each 60 carriers tested for each batch tested.

Process for Registering Antimicrobial Pesticides

- All product specific data is reviewed by Agency scientists. Label reviews are conducted by both the scientists and regulatory reviewers. If the data is found to be acceptable, the product is considered eligible for registration.

Pesticide Labels

Reading the Label

- **The Label is the Law**
  - Provides pertinent information to ensure the product is use safely and effectively.
  - Important to read the entire label.

Reading the Label

- **Labeling must bear directions for each recommended use. The directions for use must include the following:**
- **The major area(s) in which the product is recommended for use (e.g. homes, schools, hospitals).**

- **Identification of the type of surfaces, objects, or items intended for treatment (e.g. floors, walls, bathroom fixtures, medical equipment surfaces), in addition to any description of surface composition (e.g. stainless steel, chrome, glass, vinyl).**

- **The necessity for removal of gross filth or heavy soil. In addition, instructions must be provided for thorough cleaning of surfaces prior to application of the product, unless the product has been shown to be effective in the presence of moderate amounts of representative soil. Cleaning instructions must be clearly separated from the directions for use of the product as an antimicrobial agent.**

- **If the product is to be diluted, the recommended use dilution and instructions for preparing it. The units of measure (e.g. tablespoons, ounces, quarts, gallons) to be employed in diluting the product must be given, and must be understandable to the user.**

Reading the Label

- **The method(s) of application (e.g. "by sponge, mop, or spray" or "by immersion in the solution", followed by a statement such as "to wet all surfaces thoroughly").**

- **The contact time necessary for effectiveness. The directions must also indicate if, and how, the product should be removed from the surfaces after the recommended exposure period.**

- **The number of times or duration of time a prepared use solution may be used for immersible items (e.g. whether a fresh solution should be prepared for each batch or for each day's use if the solution does not become diluted or soiled, or whether the solution may be re-used for a given number of batches or for a given number of days).**

- **Additional instructions may be recommended by the applicant, or required by the Agency, as determined on a case-by-case basis.**

Reading the Label
Front Panel

1:128 E Z One-Step Hospital Disinfectant

Bactericide-Virucide*-Tuberculocide- Fungicide

Active Ingredients:

Component A 10.50%
Component B 4.25%
Component C 3.00%
Inert Ingredients 82.25%

KEEP OUT OF REACH OF CHILDREN
Warning
Net Contents

Reading the Label
Front or Back Panel

- **EPA Registration Number**
  - **Primary Registration**
    - EPA Reg. No. 123-45
  - **Distributor Registration**
    - EPA Reg. No. 123-45-6789
  - **Establishment Number**
    - 123-MD
  - **Company Address**

    Local Disinfectant Company

    555 Bacteria Count Way

    Petri Dish, State 30846

Reading the Label
Back Panel

- **Precautionary Statements**
  - Hazards to humans and domestic animals.
- **First Aid (Statement of Practical Treatment)**
  - First aid for various routes of exposure due to accidental exposure.
- **Environmental Hazards**
  - Hazards and precautions for non-target organisms
- **Physical or Chemical Hazard**
  - Flammability, Explosive potential, etc, and precautions to be taken.
- **Storage and Disposal**
- **Warranty Statement**
- **Worker Protection Labeling**

Reading the Label
Back Panel

- **Directions for Use**
  - It is a violation of Federal law to use this product in a manner inconsistent with its labeling.
- To clean and disinfect in one step: Dilute product **1 oz per gallon** of **400 ppm hard water**. Apply product by sponge, mop, cloth, or coarse spray to surface until thoroughly wet. Allow surface to remain wet for **10 minutes**. After 10 minutes, surface may be wiped dry or allowed to air dry. For surfaces that are heavily soiled, a pre-cleaning step is required. When tested according to the AOAC Use-Dilution Test, this product has demonstrated effectiveness against *Staphylococcus aureus*, *Salmonella enterica* and *Pseudomonas aeruginosa*.
- When used as directed, this product is effective against *HIV-1, Influenza A Hong Kong, Herpes Simplex 1 Virus.

Recent Public Health Initiatives

Addressing *Clostridium difficile*

- *Clostridium difficile* became an increasing public health concern between 2007 and 2008.
- Outbreaks of *C. difficile* diarrhea are not uncommon in hospitals and outpatient facilities where contamination with spores is prevalent, however the frequency of these outbreaks appears to be increasing.

Addressing *Clostridium difficile*

- In September 2008 the Agency determined that pesticide products that were efficacious only against the vegetative form of the organism may cause unreasonable adverse effects on health and the environment.
- The Agency also believed that these products might increase rather than limit *C. difficile* spore contamination -- even if used in accordance with all label directions.
- Label statements for effectiveness against vegetative C. difficile are now considered false and misleading.
- Registrants are required to amendment their labels to remove the claim against vegetative *C. difficile*.

Addressing *Clostridium difficile*

- After reviewing recommendations from the FIFRA Science Advisory Panel, the Agency released new efficacy guidance for *C. difficile* claims in early 2009.
- Guidance can be found at: http://www.epa.gov/oppad001/cdif-guidance.html
- This interim guidance is being used now to evaluate the effectiveness of any product applying for a *C. difficile* claim.
- To date, the Agency has registered one product with a label claim against *C. difficile* spores.
- The Agency anticipates receiving other registration applications in the near future.

Addressing *Clostridium difficile*

- AD launched a comprehensive effort to open a dialogue with our healthcare partners (i.e. ASHES, APIC, SHEA) and CDC in discussing the control of *C. diff* in hospital settings
- AD has also been reaching out to its various healthcare partners and hospital associations to better understand issues related to antimicrobials and hospital infection control programs
- AD is outlining plans to work more closely with the Office of Pollution Prevention and Toxics (OPPT) to coordinate national outreach and education efforts with their "Partnership for Sustainable Healthcare" Program
  - Regional meetings are also being coordinated

Antimicrobial products effective against 2009-H1N1 flu

- **Currently over 500 products are registered for use against influenza A viruses.**

- EPA believes, based on available scientific information, that these registered influenza A products will be effective against the 2009 H1N1 flu strain, and other influenza A strains.
- For safe and effective use of these products, always follow the label instructions, paying special attention to the product's dilution rate (if applicable), and contact time.
- You should choose a product whose label indicates effectiveness against "Influenza A" and lists your specific site of concern, such as; hospitals and other healthcare facilities, schools, offices, or homes.
- http://www.epa.gov/oppad001/influenza-a-product-list.pdf

Antimicrobial Testing Program

- EPA's Antimicrobials Testing Program has been conducting post-registration testing of hospital sterilants, disinfectants and tuberculocides since 1991
- Program designed to help ensure that products in the marketplace are as effective as when they were registered
- Since the program was started, EPA has tested over 335 products, just under one half of the targeted primary registrations in the testing program
- Of the tested products, slightly over one third of the disinfectant products and almost half of the tuberculocide products did not fully meet the performance standard for efficacy.

Antimicrobial Testing Program

- Understanding the specific cause of these seemingly significant percentages of products not meeting post registration standards has been elusive.
- The qualitative tests method used appears to be sensitive to even the slightest changes in protocol.

Antimicrobial Testing Program

- When a product does not meet the Agency's efficacy performance standard, one of two courses of action is pursued.
  1. An Enforcement Case Review may be developed and forwarded to the Office of Enforcement and Compliance Assurance, or
  2. A regulatory action within the Pesticide Program may be undertaken.
- In either case, the goal is to bring the product back into compliance.
- To ensure product performance, AD will now require confirmatory efficacy data for products subject to an enforcement or regulatory action to resolve the ATP efficacy failure and to return products to commerce.
- Efforts are underway to accelerate confirmatory efficacy testing of public health pesticide via the antimicrobial testing program (ATP).

Antimicrobial Testing Program

- The Agency is also looking at further modifications to the program and is open to ideas to make long-term testing more effective -- Some thoughts include:
  - Changes in the way the testing is conducted
  - Making the information available to the public more quickly
  - Working with the various health associations and Hospital associations on training
  - Additional information and status of products tested can be found at http://www.epa.gov/oppad001/antimicrobial-testing-program.html

Future Directions

Increased coordination with all stakeholders

Exploring best ways to reach out to hospital and public health community

AD is seeking to start an open dialogue with all those involved with ensuring the protection of public health in our nation's hospitals, HMO's, clinics, nursing homes, and urgent care facilities.

It is our desire to better understand how disinfectant products are being used in these settings and how we might be able to work better with all public health facilities.

Review of Goals

- Presented an overview of the Antimicrobials Division.
- Described antimicrobial pesticides and pests.
- Reviewed the importance of reading and understanding a pesticide label.
- Highlighted key public health initiatives.

Questions/Comments/ Discussion

Thank You

Additional Information

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- Regulating Pesticides: http://www.epa.gov/pesticides/regulating/index.htm
- Regulating Antimicrobial Pesticides: http://www.epa.gov/oppad001/