AGENDA

FIFRA SCIENTIFIC ADVISORY PANEL (SAP)
OPEN MEETING

July 17 - 19, 2007

FIFRA SAP WEB SITE http://www.epa.gov/scipoly/sap/
OPP Docket Telephone: (703) 305-5805
Docket Number: EPA-HQ- OPP-2007-0186

U.S. Environmental Protection Agency
Conference Center - Lobby Level
One Potomac Yard (South Bldg.)
2777 S. Crystal Drive, Arlington,VA 22202

Guidance on Test Methods for Demonstrating the Efficacy of Antimicrobial Products for Inactivating *Bacillus anthracis* Spores on Environmental Surfaces

Tuesday, July 17, 2007

8:30 A.M. **Introduction and Identification of Panel Members** - Steven G. Heeringa, Ph.D. (FIFRA SAP Chair)

8:40 A.M. **Administrative Procedures by Designated Federal Official** - Mr. Joseph E. Bailey, Office of Science Coordination and Policy, EPA

8:45 A.M. **Welcome and Opening Remarks** – Debbie Edwards, Ph.D., Director, Office of Pesticide Programs, EPA

8:50 A.M. **Introduction and Background** - Jeff Kempter, Antimicrobials Division, Office of Pesticide Programs, EPA

9:15 A.M **Sporicidal Activity of Disinfectants (AOAC Method 966.04)** - Stephen Tomasino, Ph.D., Microbiology Laboratory Branch, Biological and Economic Analysis Division, EPA

10:00 A.M. **Break**

10:15 A.M **Overview of Lab-Scale Quantitative Test Methods for Sporicidal Decontamination Agents** - Stephen Tomasino, Ph.D., Microbiology Laboratory Branch, Biological and Economic Analysis Division, EPA

11:00 A.M **Quantitative Test Methods for Evaluation of Sporicidal Fumigants in Relation to Military-relevant Material Surfaces –** Vipin Rastogi, Ph.D., Edgewood Chemical and Biological Center (ECBC), Department of Defense

11:30 A.M. **EPA's Proposed Measure of Success for Quantitative Sporicidal Efficacy Test Results -** Marty Hamilton, Ph.D., Professor Emeritus, Montana State University

12:00 P.M. **Lunch**

1:15 P.M. **Coupon Materials for Lab-Scale Quantitative Test Methods for Sporicidal Decontamination Agents -** Stephen Tomasino, Ph.D., Microbiology Laboratory Branch, Biological and Economic Analysis Division, EPA

2:00 P.M. **Surrogate Selection and Attributes for *Bacillus anthracis* Spores-** Stephen Tomasino, Ph.D., Microbiology Laboratory Branch, Biological and Economic Analysis Division, EPA

2:45 P.M. **Break**

3:00 P.M. **Molecular Differentiation of Virulent *Bacillus anthracis* from Avirulent Related Surrogate Strains -** Vipin Rastogi, Ph.D., Edgewood Chemical and Biological Center (ECBC), Department of Defense

3:30 P.M. **NHSRC Research on Decontamination of *Bacillus anthracis* and Surrogate Spores on Building Material Surfaces -** Joe Wood, M.S., P.E., and Shawn Ryan, Ph.D., National Homeland Security Research Center, EPA

4:30 P.M. **Simulated Use Test -** Michele Wingfield, Antimicrobials Division, Office of Pesticide Programs, EPA

5:00 P.M. **Adjournment**

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8:30 A.M. **Introduction and Identification of Panel Members** -
Steven G. Heeringa, Ph.D. (FIFRA SAP Chair)
8:40 A.M. **Administrative Procedures by Designated Federal Official** -
Mr. Joseph E. Bailey, Office of Science Coordination and Policy, EPA
8:45 A.M. **Public Comments**
10:00 A.M. **Break**
10:15 A.M. **Charge to Panel - Issue 1**

Whether a sterilant or sporicide product may claim that it inactivates *B. anthracis* spores on inanimate surfaces.

EPA's existing efficacy testing guidance specifies that a product that passes the AOAC Sporicidal Activity of Disinfectants test (AOAC Official Method 966.04) may be registered as a sterilant/sporicide. The Agency is now proposing that a sterilant/sporicide may also bear a claim that it inactivates *B. anthracis* spores if it passes confirmatory testing using the AOAC 966.04 with virulent *B. anthracis* spores on carriers made of porcelain penicylinders and silk loops, which represent nonporous and porous surfaces, respectively.

The rationale for EPA's position is that the AOAC Method and associated EPA performance criteria (e.g., no growth from any carriers tested) have been required historically by EPA for evaluating the performance of sporicidal chemicals for

regulatory purposes. The AOAC Method specifies the use of two spore-forming microbes, *B. subtilis* and *Clostridium sporogenes;* however, the Agency believes that the method is also suitable for testing spores of other spore-forming bacteria such as *B. anthracis*. The Agency has recognized deficiencies in the AOAC 966.04 Method and has improved the procedure through the official AOAC modification process – the modifications appear in AOAC 966.04 Method II. The Agency strongly prefers the use of the Method II to support the registration of sterilants/sporicides and for confirmatory testing of *B. anthracis*. In addition, the Agency has successfully revised the method editorially (see Method II), thus providing a more standardized protocol for use by stakeholders. The modifications are presented in AOAC 966.04 Method II. See Reference 1 for the entire method; see References 2 and 3 for experimental details.

<u>Charge Question 1</u>: Please comment on the scientific basis that confirmatory testing of a sporicide/sterilant using AOAC Method 966.04 with virulent *B. anthracis* spores demonstrates that a product inactivates *B. anthracis* spores on inanimate surfaces.

11:15 A.M. Charge to Panel - Issue 2

Whether a sporicidal decontaminant product may claim that it inactivates *B. anthracis* spores on inanimate surfaces, when tested solely with AOAC Method 966.04 using virulent *B. anthracis* spores.

The Agency is proposing that an antimicrobial product may be registered as a "sporicidal decontaminant" if it is tested with the AOAC Method 966.04 using virulent *Bacillus anthracis* spores (instead of *B. subtilis* or *C. sporogenes*), or using a surrogate acceptable to EPA, on porcelain penicylinders and/or silk loops, which represent nonporous and porous surfaces, respectively. The Agency's rationale is consistent with the use of the AOAC 966.04 method for sterilant/sporicidal agents; however, the Agency will not require registrants to conduct the entire AOAC Method 966.04 to support a sporicidal decontaminant claim. The Agency believes that product efficacy against spores of *C. sporogenes*, an anaerobic spore-forming species relevant to clinical environments, has limited applicability to decontamination scenarios involving spores of *B. anthracis,* and thus testing against *C. sporogenes* will not be required. Furthermore, the registrant will be allowed to test against porcelain and/or silk loops (which represent nonporous and porous surfaces, respectively) depending on the proposed claims. Continued use of EPA product performance criterion (e.g., no growth from any carriers tested) is appropriate for testing the efficacy of sporicidal decontaminants against spores of *Bacillus anthracis.*

<u>Charge Question 2</u>: Please comment on the scientific basis that use of the AOAC Method 966.04 with virulent *B. anthracis* spores demonstrates that a sporicidal decontaminant product inactivates *B. anthracis* spores on inanimate surfaces.

12:15 P.M. Lunch
1:30 P.M. Charge to Panel - Issue 3

Whether a six (6) log (log_{10}) reduction is an adequate measure of success when employing a well developed, quantitative sporicidal efficacy test.

The Agency is proposing that an antimicrobial product may be registered as a "sporicidal decontaminant" if it is tested using a well developed, quantitative sporicidal test method acceptable to EPA using virulent *Bacillus anthracis* spores (or a surrogate acceptable to EPA) on nonporous and/or porous inanimate surfaces and the testing of the product achieves at least a six (6) log reduction (or a minimum 1×10^6 spores per carrier) of virulent *B. anthracis* spores (or a surrogate acceptable to EPA). The use and adoption of standardized quantitative methods for testing the performance of sporicidal decontaminants for regulatory purposes is supported by EPA. The AOAC Method 966.04 is a qualitative procedure (i.e., provides only positive/negative or pass/fail results). Quantitative procedures provide an estimate of actual spore kill, usually based on the log_{10} scale, and can be adapted for multiple product formulations and carrier materials. Several well-developed quantitative procedures are available for use. The Agency believes that a performance standard for quantitative laboratory-based assays is essential to establishing consistent product efficacy under actual decontamination scenarios in the field. The proposed 6 log reduction performance standard is a scientifically valid and rigorous standard. The standard will give the Agency reassurance that sporicidal decontaminants when applied per the product's label claims are effective against spores of *B. anthracis.*

The technical basis of the Agency's selection of a minimum 6 log performance standard includes the following:

(1) the target spore titer currently allowed in AOAC method 966.04 (Method II) is a minimum of 1×10^5 to approximately 1×10^6 spores per carrier) (Reference 1);

(2) the quantitative methods currently available and published can reliably generate control carrier spore titers necessary to measure a 6 log reduction (for examples of quantitative methods, please see the following: ASTM E 2111-05 (Reference 4); Standard Quantitative Disk Carrier Test Method, ASTM E 2414-05: Standard Test Method for Quantitative Sporicidal Three-Step Method (Reference 5); Standard Quantitative Carrier Test Method, ASTM E 2197-02 (Reference 6); and also References 7 and 8);

(3) a minimum 6 log reduction in viable spores has been measured for commercially available sporicidal agents and technologies designed for treating sites contaminated with *B. anthracis* (see References 9-13); and

(4) environmental sampling pre- and post-application of the sporicidal decontaminant will determine the need for re-treatment.

Charge Question 3: Please comment on the scientific basis that achieving a six (6) log reduction using a well developed, quantitative sporicidal test method demonstrates that a product inactivates *B. anthracis* spores on inanimate surfaces.

2:30 P.M. Break
2:45 P.M. Charge to Panel - Issue 3.1

What criteria should be used when selecting coupon materials for quantitative sporicidal tests.

The Agency is proposing to allow only certain nonporous and porous materials to be used in the quantitative sporicidal tests based on specific criteria. The rationale for EPA's position is that in order to achieve reproducible results across laboratories, and to ensure that test materials are suitable to support a particular claim (i.e., material type to be treated), basic criteria should be established. The EPA also recognizes that the nature of the test material may impact product performance. The criteria that EPA intends to establish for the selection of carriers and carrier materials include the use of standardized materials (e.g., quality, grade and consistency), relevancy of materials to the use site, material availability, data on spore recovery, ability to clean and sterilize prior to inoculation, and potential for interaction with the product's active ingredients.

Charge Question 3.1: Please comment on the EPA's criteria for selecting coupon materials to represent nonporous and porous surfaces in quantitative sporicidal efficacy tests.

3:45 P.M. Charge to Panel - Issue 4

Whether a surrogate *Bacillus* species of spores may be used in place of *Bacillus anthracis* spores in sporicidal efficacy tests.

The Agency is proposing to allow certain surrogate, avirulent *Bacillus* species to be used in place of virulent *Bacillus anthracis* spores for either qualitative or quantitative sporicidal efficacy tests based on specific criteria. Surrogate spores should have certain desirable attributes and be acceptable to EPA. The use of safe-to-handle surrogates of virulent *B. anthracis* spores is supported by the EPA. Surrogates are frequently used as models or representatives for virulent strains of pathogens such as *B. anthracis* Ames. Federal restrictions and bio-safety issues limit the number of labs capable of testing select agents. Cost, time and resources required for managing studies on virulent *B. anthracis* spores are also limiting factors. Certain criteria should be met in order for a surrogate to be utilized in the efficacy testing of sporicidal decontaminants. To be an acceptable surrogate, a *Bacillus* spore species should generally be as resistant or more resistant to inactivation by a particular chemical on a particular surface than *B. anthracis* spores.

To demonstrate equivalent resistance of the surrogate spore type to the virulent agent, a comparative efficacy study should be performed using a well-developed/validated quantitative methodology appropriate for the test chemical and microbe to measure resistance. Testing should be conducted in accordance with the potential product claim. Replicated studies with adequate controls and with side-by-side, parallel test designs are desirable. It is also desirable to compare carriers with comparable spore populations. The same sporulation media should be utilized for all test microbes. Percent recovery of spores from carriers should be determined in advance. The strain of *B. anthracis* used in the study should be verified as a pathogenic strain. Examples of acceptable and relevant surrogate studies are provided in References 7 and 8. Pre-existing data may be appropriate to support the use of a surrogate as well.

<u>Charge Question 4</u>: Please comment on the desirable attributes for selecting surrogate *Bacillus* species for *Bacillus anthracis* in either qualitative or quantitative sporicidal efficacy tests.

5:00 P.M. Adjournment

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Steven G. Heeringa, Ph.D. (FIFRA SAP Chair)

8:40 A.M. **Administrative Procedures by Designated Federal Official** -
Mr. Joseph E. Bailey, Office of Science Coordination and Policy, EPA

8:45 A.M. **Charge to Panel - Issue 5**

Whether gas or vapor products should be subjected to a "simulated use test."

The Agency is proposing that gas or vapor sterilants, sporicides and sporicidal decontaminants be subjected to a "simulated use test" for gas or vapor products intended for use in large, enclosed spaces. The rationale for EPA's position is that efficacy testing performed in the laboratory does not necessarily demonstrate that a product will perform satisfactorily when applied in a large, enclosed space. Many factors can reduce the effectiveness of a gas or vapor product, such as inadequate distribution, breakdown by light, and absorption/breakdown by porous or reactive surfaces. Accordingly, EPA believes that a simulated use test is needed to demonstrate that a gas or vapor product will perform successfully in a large volume of space (e.g, a typical office). In addition, such a test should include monitoring to assure that key parameters (e.g., temperature, relative humidity, concentration) for an effective fumigation will be met.

Charge Question 5: Please comment on the scientific basis for conducting a "simulated use test" for a gas or vapor product intended for use in large, enclosed spaces.

10:00 A.M. Break
10:15 A.M. Continued Panel Discussion (as needed)
12:00 P.M. Lunch
1:15 P.M. Continued Panel Discussion (as needed)
2:45 P.M. Break
3:00 P.M. Continued Panel Discussion (as needed)
5:00 P.M. Adjournment

Please be advised that agenda times are approximate; when the discussion for one topic is completed, discussions for the next topic will begin. For further information, please contact the Designated Federal Official for this meeting, Mr. Joseph Bailey, via telephone: (202) 564-2045; fax: (202) 564-8382; or email: bailey.joseph@epa.gov