February 17, 2010

Tim Leighton
Office of Pesticide Programs
U.S. Environmental Protection Agency
One Potomac Yard (South Building)
2777 South Crystal Drive
Arlington, VA 22202

Dear Tim:

The AEATF has reviewed the December 16, 2009 HSRB final report of October 20-21, 2009 meeting. A revised protocol in track changes that incorporates EPA and HSRB comments at the meeting and summary of changes to the protocol are attached. The AEATF also has reviewed the final HSRB report and provides the below responses to the comments on the aerosol study protocol.

The Board raised the concerns highlighted in italics below. Our response/clarification follows.

1. ***Use of the Results***: *EPA plans to use the data generated from the proposed aerosol study generically to estimate dermal and inhalation exposures and risks for other antimicrobial ingredients where the product is packaged in a pressurized aerosol spray can. However, other variables can affect rates of exposure, including different nozzle sizes, spray and ejection rates, the size of the particles generated, and the generation of nonvolatile active ingredients. Inhalation versus dermal exposure may also vary with these variables.*

   It is also unclear if occupational handler exposure can be used to estimate exposure of non-professionals using similar consumer products. However, for risk assessment purposes it was felt that exposure among occupational users is likely to exceed that of consumers; the higher frequency of exposures among occupational users is likely to exceed a plausibly higher individual but less frequent exposure among nonprofessional users.

   Response: We agree that dermal and inhalation exposure risks to antimicrobial ingredients delivered using a pressurized aerosol spray can will be impacted by different nozzle sizes, spray and ejection rates, the size of the particles generated and the generation of nonvolatile active ingredients. The aerosol products represented by the AEATF II have been divided into four major use categories:

   1. Hard-surface disinfectant fine sprays
   2. Foaming aerosol products
   3. Soft surface disinfectants
   4. Air fresheners

Prior to selecting a product that represents the four major use categories, keeping in mind that we wanted to select a product that represents an inhalation exposure worst-case situation, a non-human pilot study was conducted. In that study, one representative and commercially available product was selected from each category. The study design and results of the pilot study were presented in Appendix A of the Aerosol Application Scenario: Rationale for Study Design. The results of the pilot study clearly show that the hard-surface fine spray and the air freshener used generated the most inhalation and/or dermal exposure potential. The total mass of the active ingredient dispensed per unit time for the hard-surface fine spray is more than double the air freshener; based on that information, inhalation and dermal exposure will likely be higher for the hard surface fine spray. Additionally, the hard-surface spray product will be used to a much greater extent in a day, especially in commercial use, than the air freshener. Based on the available data, the hard-surface fine spray would represent a high and conservative choice for exposure monitoring studies. The selected product should also meet objectives of the study and test material selection criteria, i.e.:

- Serve as surrogate for most aerosol use categories
- Use pattern represents high-end exposure – a conservative scenario
- Use scenario covers most influential variables of exposure
    - Highest percentage of active ingredient
    - Nozzle size of majority of aerosol products
    - Particle size distribution representative of fine spray
    - Used for hard surface and confined spaces
- Having stable active ingredient
- Results can be extrapolated to most products on the market

Since the goal of this study is to select one surrogate for most aerosol use categories, the product selected for this study was a hard-surface disinfectant fine spray, the "Clorox Disinfection Spray."

We agree with the HSRB regarding occupational handler exposure and non-professional exposure.

2. ***Sample Size and Analysis***: *Raw and descriptive data will be provided, but no statistical analyses have been planned. Sample size adequacy cannot be judged without a statistical analysis plan. Placing 18 subjects into three clusters of six each requires consideration of cluster effects and may complicate analysis of the results. Assumed constants related to exposure to the active ingredient may also prove to be incorrect, and additional subjects may need to be enrolled.*

Response: If the benchmark accuracy goal (i.e., K=3) is not met once the data are collected and analyzed, the AEATF II will, in consultation with regulatory agencies, determine the best course of action to take. This may mean the development of guidance for the use of these data that takes the increased imprecision of the estimates into account. It is possible that collection of additional clusters might be considered.

3. ***Application of Spray****: The target number of cans sprayed in each location by each worker on each day could be specified better within the protocol. For example, does a worker need to continue spraying a room if the target application is met before completion of that room? Additional protocol clarifications needed include: addressing the issue of the interval between sampling at different sites (currently, it appears that no two monitoring events can occur within the same building within one week); clarifying the issue of using empty apartments rather than motel rooms; and clarifying the effect of exhaust vent effects on exposure, which could be different than indicated in the protocol.*

   Response: We will clarify in the protocol the target numbers of cans sprayed in each location by each worker on each day. Workers will be given full cans as well as half full cans, as specified in the protocol. A worker does NOT need to continue spraying a room if the target application is met. Two monitoring events can occur within the same building, but not the same room within ONE DAY. The next day the same room could be used. Regarding the use of apartments rather than motel rooms, we have surveyed the Fresno area and have found a number of motels with full kitchens. We will be using hotels/motels exclusively for the study and will not be using apartments.

4. ***Quality Assurance and Control (QA/QC)*****:** *QA/QC can be improved by:*

   a. Determining likely differences in the air sampling results depending on the method used (e.g., depending on the air sampling equipment used, differences in the orifice diameters and air flow sampling rates could affect aerosol collection efficiencies and effects).

   b. Setting the minimal spike to two to four times that of the limit of quantitation (LOQ; cf. AEATF II 2009b: 42, 46).

   c. Considering other variables that may influence the measurement of exposure, including whether the surface being treated is dry or wet at the time of the next spray application, and whether the applicant accidentally wiped the surface after spraying. Data accumulated during gross deviations from the protocol should also be excluded. Finally, the protocol should indicate that there will be a maximum of two workers on any given day in the same location.

Response:

a. The determination of differences in air sampling results based on the difference in the orifice diameter, etc., would imply comparing different products. This is not in the scope of this study since we will be using one product. In this study, we will be using the same sampling equipment for all subjects. The equipment will be calibrated daily for air flow sampling rate.

b. The LOQ for field fortification will be corrected. The minimum spike of four times the LOQ will be incorporated in the protocol.

c. At the time of application, all treated surfaces will be dry. The same room will be treated three times on three separate days. The goal is to have two ME/day/locations, and complete the application of the product to different rooms. Back-up workers will also be available in case the primary worker does not show up.

If you have any questions, please contact me at (703) 741-5637 or via email at has_shah@americanchemistry.com.

Sincerely,

Hasmukh Shah

Hasmukh Shah
Manager, AEATF

Cc: John Carley
Kelly Sherman