Minutes of the
United States Environmental Protection Agency (EPA)
Human Studies Review Board (HSRB)
January 17, 2013 Public Meeting
Docket Number: EPA-HQ-ORD-2012-0892
HSRB Website: http://www.epa.gov/osa/hsrb

Committee Members: (See EPA HSRB Members List—Attachment A)

Date and Time:	Thursday, January 17, 2013, 1:00 – 5:00 PM (See *Federal Register* Notice—Attachment B)	
Location:	EPA, One Potomac Yard (South Building), 2777 S. Crystal Drive, Arlington, VA 22202	
Purpose:	The EPA HSRB provides advice, information and recommendations on issues related to the scientific and ethical aspects of human subjects research.	
Attendees:	Chair:	Rebecca T. Parkin, Ph.D., M.P.H.
	Vice Chair:	Jewell H. Halanych, M.D.
	Board Members:	George C.J. Fernandez, Ph.D. Sidney Green, Jr., Ph.D., Fellow, ATS Elizabeth Heitman, Ph.D. Dallas E. Johnson, Ph.D. John C. Kissel, Ph.D. José E. Manautou, Ph.D. William J. Popendorf, Ph.D. ^Nu-May Ruby Reed, Ph.D., D.A.B.T. Leonard Ritter, Ph.D., ATS Virginia Ashby Sharpe, Ph.D. Linda J. Young, Ph.D.
Meeting Summary:	Meeting discussions generally followed the issues and general timing as presented in the meeting Agenda (Attachment C), unless noted otherwise.	

Commencement of Public Meeting and Review of Administrative Procedures

Mr. Jim Downing (Designated Federal Officer [DFO], HSRB [or Board], Office of the Science Advisor [OSA], EPA [or Agency]) convened the meeting at 1:00 p.m. and welcomed Board members, EPA colleagues and members of the public. He thanked the Board members for their work in preparing for the meeting deliberations.

Mr. Downing noted that in his role as the DFO under the Federal Advisory Committee Act (FACA), he serves as liaison between the HSRB and EPA and is responsible for ensuring that

all FACA requirements are met. The DFO must work with appropriate Agency officials to ensure that all appropriate ethics regulations are satisfied regarding conflicts of interest; HSRB members have been briefed on federal conflict of interest laws and have completed a standard government financial disclosure report. In consultation with the deputy ethics officer for OSA and the Office of the General Counsel, Mr. Downing has reviewed the reports to ensure that all ethics requirements are met.

Mr. Downing informed members that there is an interesting and significant topic on the agenda for the meeting. He noted that agenda times are approximate, and the group will be kept to those times as closely as possible. All speakers, including Board members and members of the public, should use their microphone and identify themselves before speaking, as the meeting is being recorded and broadcast on the Internet. During Board discussions, if members require clarification from the public, they may request such information through the Chair or DFO. Copies of the meeting materials, supporting documents and public comments will be available at http://www.regulations.gov under docket number EPA-HQ-ORD-2012-0892 and most are available on the HSRB website at http://www.epa.gov/osa/hsrb. Following the presentations, time has been scheduled for questions of clarification to EPA staff and the principal investigator and sponsors of the studies. This time is to be used for points of clarification rather than Board discussion. A public comment period will be maintained, and remarks must be limited to 5 minutes. No members of the public had pre-registered to make a public comment for the topic under consideration. Meeting minutes, including a description of the matters discussed and conclusions reached by the Board, will be prepared and must be certified by the meeting Chair within 90 days. The HSRB also will prepare a final report in response to questions posed by the Agency that will include the Board's review and analysis of materials presented. EPA will announce in the *Federal Register* a public conference call meeting for the Board's review and subsequent approval of the Final Report. Mr. Downing turned the meeting over to the HSRB Chair, Dr. Rebecca Parkin.

Introduction and Identification of Board Members

Dr. Parkin welcomed the Board members and said a new member, Dr. Nu-May Ruby Reed, would be monitoring the meeting via teleconference. She asked Board members to introduce themselves, and members completed their introductions. Dr. Parkin next referred to Mr. Downing, who invited Dr. Glenn Paulson (Science Advisor, EPA) to offer welcoming remarks.

Welcoming Remarks

Dr. Paulson welcomed all in attendance to the first HSRB meeting of 2013. One of the responsibilities of the Science Advisor is to provide administrative oversight of the workings of the HSRB, which is a FACA committee. For the first time since the HSRB was created, the EPA Science Advisor has only one set of duties, albeit wide ranging. Prior to his appointment, the Science Advisor and the Assistant Administrator for the Office of Research and Development (ORD) was the same person. The duties of these positions now are divided equally between two people. Dr. Paulson indicated that he would be happy to answer any questions about his broader responsibilities. He joined Mr. Downing and Dr. Parkin in expressing appreciation to the Board members for their service in preparing, participating and following up for this meeting. As a

former member of many federal committees, he recognized and appreciated both the time required and the amount of material reviewed to prepare for the deliberations during the meeting. He also appreciated the Board's commitment to these issues in view of other obligations. Dr. Paulson welcomed members of the public and thanked the Office of Pesticide Programs (OPP), OSA and other EPA colleagues for the work leading up to this formal public meeting.

Dr. Paulson next noted changes to the Board. He welcomed Dr. Parkin, who has been a Board member since October 2007 and previously served as interim Vice Chair, in her new role as Chair through August 2013. He remarked that the EPA team looks forward to working with her in her capacity as Board Chair to advise EPA on scientific and technical issues regarding third-party research on human subjects. In addition, Dr. Jewell Halanych will serve as the Board's Vice Chair through August 2014. Dr. Paulson also welcomed three new members, noting EPA's appreciation at their acceptance to serve on the HSRB and anticipation to access their expertise in reviewing ethical and scientific issues. The three new members were introduced as follows:

- Dr. Elizabeth Heitman, Vanderbilt University, has faculty appointments in the Department of Medicine's Division of General Medicine and Division of Critical Care, as well as in the Department of Religious Studies. Her work focuses on the cultural and religious aspects of medicine, biomedical science and public health, particularly regarding education and community experience. Her primary research addresses the evaluation of education and research ethics, responsible conduct of research, and cultural awareness of professional socialization of students and researchers. She serves as the Co-Chair of the Ethics Committee and a member of the Critical Care Committee and the Organ Donation Advisory Committee at the Vanderbilt University Medical Center.

- Dr. John Kissel is a Professor of Environmental and Occupational Health Sciences at the University of Washington. He holds a Ph.D. in civil and environmental engineering and is a registered Professional Engineer. His research involves human exposure assessment related to waste management practices, including agricultural and residential use of pesticides and consumer products. His current interest relates to probabilistic predictions of human exposure and the reconciliation of predictions with biomarker data.

- Dr. Nu-May Ruby Reed is a recently retired toxicologist from the California EPA (Cal/EPA) Department of Pesticide Regulation, where she served as the lead scientist in risk assessment issues. Her research interests include evaluating health risks and developing pesticide risk assessments. She also has represented her Department regarding community concerns and emergency response.

Dr. Paulson informed members that on December 19, 2012, he met with a group of experts in human subjects protection, co-chaired by Dr. Mary Swigar, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey, to review and evaluate EPA's Human Subjects Research Program and provide recommendations to EPA to strengthen the Agency's program for the protection of human research subjects in future years. The retirement of Dr. Warren Lux, the Human Subjects Research Review Official (HSRRO), seemed an appropriate time to review and reevaluate EPA's program for human subject protections. This group of experts will meet again in March 2013 to provide their recommendations.

EPA will announce the position of HSRRO later in January 2013. A search committee has been established and will evaluate applications for this critical position. Dr. Paulson noted that Board members already had received this announcement and were asked to disseminate this information to procure a strong list of potential candidates for the position.

Dr. Paulson next reviewed the main topic for consideration at this meeting, which is the completed study from the Antimicrobial Exposure Assessment Task Force II (AEATF) in which the dermal and inhalation exposure of professional janitorial workers was monitored as they poured liquid antimicrobial pesticide products from conventional or reduced-splash containers into different sizes and types of source containers. EPA seeks the HSRB's advice regarding: (1) the scientific soundness of this completed research and on its appropriateness for use in estimating exposure that results from pouring liquid antimicrobial pesticide products; and (2) whether available information supports a determination that the study was conducted in substantial compliance with subparts K and L of 40 Code of Federal Regulations (CFR) part 26. He reminded the Board that it had considered the protocol for this study at its October 2011 meeting and now has the opportunity to review the completed study and provide expert advice and recommendations to EPA.

Dr. Parkin thanked Dr. Paulson for his comments, which offer a new context for Dr. Paulson's responsibilities, and said that she and the Board looked forward to working with him.

Opening Remarks

Dr. Steven Bradbury, Director, OPP, Office of Chemical Safety and Pollution Prevention (OCSPP), EPA, welcomed attendees to the meeting and expressed his appreciation for the Board's efforts to help EPA move forward. From EPA's perspective, the advice and input received from the Board has demonstrated that high-quality research can be performed that adheres to high standards and ethical conduct. The input from the Board is instrumental in facilitating the path forward. The improved quality of protocols and research plans submitted to the HSRB over the years is a reflection of the Board's efforts and input. Investigators have learned how to better document protocols and explain their approach, ensuring high-quality science, ethics and standards.

The HSRB's advice has helped EPA undertake internal reviews. It is clear that the concepts and insights are penetrating throughout the Agency, such as when staff scientists seek advice. Another important aspect is the concept of public participation and transparency, as input and comments from the public are critical. EPA makes special efforts to listen to the public so that everyone has confidence that the activities undertaken will ensure high-quality science and the highest ethical standards.

Dr. Bradbury also welcomed the new Board members to this effort and thanked Drs. Parkin and Halanych for assuming their HSRB leadership roles. He echoed Dr. Paulson's appreciation for the amount of work required for these meetings, including efforts by Mr. Downing and OSA staff in preparing for the meeting. EPA also appreciates the work in preparing the Board's report and for all input received from the Board, EPA colleagues and the public.

Dr. Parkin added her gratitude to the EPA staff. She noted that this meeting and agenda item had been delayed because Hurricane Sandy in November 2012 had prevented a quorum of Board members from attending, and she encouraged all to remember the people who still are affected deeply by that storm.

OPP Follow-Up on Previous HSRB Recommendations

Dr. Parkin welcomed Mr. William Jordan (OPP, EPA) to present the follow-up of the Board's previous recommendations. Mr. Jordan provided a brief overview of the context that led to the Board's review of the AEATF study report to communicate how the information that resulted from the study will be used. He indicated that he would first provide an overview of the regulatory framework and then turn to specific aspects of the study.

In terms of the statuary framework, EPA regulates pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). FIFRA requires that every pesticide product sold in the United States undergo an approval process called registration. The registration process addresses composition, labeling and packaging separately. Composition includes a defined statement of the formula (i.e., the percentage of active and inert ingredients) as well as the type of formulation (e.g., liquid, dust, granule, gas). EPA spends most of its time on the labeling of pesticides. Each pesticide product contains labeling—that is, written instructions for use. These directions define target pests as well as the method of mixing and application information (loading, quantity, frequency and when to apply). In addition, warnings and cautions are associated with applying the product. Instructions also are included regarding special equipment, especially personal protective equipment (PPE). Other limitations, such as restricted harvesting intervals and requirements for the planting of different crops in the future year, also are described. All instructions are important because it is unlawful to use pesticides inconsistent with the labeling. The labeling is the law and guides the understanding of how a pesticide is to be used. Packaging concerns the container size, composition and other characteristics but generally is not regulated.

After EPA procures the information on composition and labeling, it then determines if the pesticide can be sold in the marketplace based on whether there are unreasonable adverse effects to the environment. The registration standard considers both the risks and benefits of using the pesticide. Pesticides provide a useful purpose to the consumer but are biologically active and also can pose risks. EPA makes a decision on whether the benefits of using the pesticide outweigh the risks; most of its focus concerns risk, which is a function of toxicity and exposure.

EPA considers a wide range of potential risks, both to human health and the environment, that arise from pesticide use. These risks include occupational, dietary, bystander and residential risks. Occupational risks include the handlers or workers that apply or work around applications of pesticides. Dietary risks include residues in food, and the objective is to ensure that foods are safe to eat. Bystander risks become important when pesticides that are applied outdoors move beyond the intended site and affect those nearby. There also are risks for people in residential settings (e.g., schools, office spaces).

Mr. Jordan stated that the completed study under review generated data for use in occupational risk, particularly for two categories: handlers and workers. Handlers are people who mix, load or apply pesticide products to the environment or home. Workers enter the area where the pesticide was applied and are exposed as a consequence of work activities to the residues that remain following the application. Handler exposure depends on three elements:

(1) How the pesticide is mixed, loaded and applied. Research aims to derive "unit exposure," that is, the amount of an active ingredient in the pesticide that a person will be exposed to while performing certain activities, and normalizing that amount of exposure to the amount handled. The handling scenario is a particular set of activities by the handler that is described by the type of pesticide (e.g., dust, wettable powder) and the activity of the person (e.g., mixing, applying, loading). Sometimes the scenarios vary according to equipment, as the type of application equipment can make a difference in the handling scenario. A person's exposure to an antimicrobial product applied to a floor might be different depending on whether a mop was used or a trigger spray bottle followed by wiping with a rag or sponge.

(2) How much of the pesticide is handled. We assumed that the more pesticide is handled, the more exposure will occur. This is why the unit exposure usually is normalized to the active ingredient, followed by an examination of how the active ingredient is handled.

(3) The impact of using PPE. The exposure to a person is affected by the clothing and PPE (e.g., chemically resistant gloves, apron, respirator) that are worn.

Mr. Jordan next described data sources for estimating occupational exposure. For unit exposures, studies with surrogate chemicals that measure inhalation and dermal exposure to the handlers' body during the activity are considered. Dermal exposures are measurements of residues on different parts of the body; for inhalation exposure, an air monitor collects residues in the breathing zone of the handler. A surrogate chemical is used because it is assumed that the exposure does not depend on what active ingredient is in the pesticide. Which chemical is used to mop a floor is less important than how the floor is mopped with water containing the chemical.

With regard to the amount of active ingredient handled (AaiH), EPA monitors the estimate at the higher end of exposure. Regarding mopping, for example, desired data would include the number of hours that a janitor or hospital orderly might spend mopping floors during a normal day's work, followed by an analysis of how many gallons of water-mop mixture that person used per hour. Finally, the pesticide label would be examined to ascertain how much active ingredient would be in each gallon of mop water. These values would be multiplied together to obtain the high-end estimate of the amount of active ingredient that a person is handling while performing the daily task.

Mr. Jordan discussed the impact of PPE. Data sources indicate the reduction of a certain percentage of exposure by inhalation if someone wears a respirator; similarly, the residue on the hands will be reduced by a certain percentage if one wears chemically resistant gloves. All of the

datasets are pooled to develop an estimate of the high-end exposure of the handler performing a task with a particular product.

The concept of unit exposure was described. The common-sense approach assumes that the more pesticide a person handles, the more exposure a person can get. A representative study ascertained individual exposure to varying amounts of pesticide. These data showed that the exposure rises as the AaiH increases. The data reflect that some people are more careful than others in handling pesticides; inter-individual variability is addressed through taking the unit exposure and finding the mean of the different values, and applying these across the data. By using conservative values for other components of the exposure, the estimate reaches the high-end values to represent handler exposure. Although the current discussion will consider a dataset that looks different, this historical dataset can be used in a way to provide a conservative estimate of high-end exposure.

Mr. Jordan advocated the use of proportionality analysis. If the unit exposure was not used to normalize to the AaiH, there would be many more studies required. The surrogate pesticide notion allows one to extrapolate from one study to many different active ingredients that are mixed, loaded or applied using the same techniques. Additionally, data are not needed regarding application rates and pesticides in the product. From the standpoint of practicality and reducing human exposure, as well as making it possible to conduct risk assessments efficiently, the notion of proportional unit exposure makes sense. One should recognize that when the line of lognormal plots of data is not exactly 1 in terms of slope, this may lead to an underestimation of exposure at lower AaiH and overestimation of exposure at higher AaiH. From a policy perspective, this is an appropriate, acceptable error because regulators do not base risk decisions on estimates of risk that are too low. If a decision that is based on too high a risk estimated under real-world conditions is acceptable, then the lower value also would be acceptable. Mr. Jordan proposed that errors introduced under the notion of proportionality are an acceptable way to approach the assessment of exposure.

Board Questions

Dr. Parkin asked Mr. Jordan to expand on the concept of what constitutes an acceptable surrogate and what types of criteria to consider or judge if a specific surrogate is an appropriate representative chemical of interest. Mr. Tim Leighton (OPP, EPA) responded that when looking at data from a surrogate, the use should be fully representative to ensure that the actual scenario (e.g., how people are exposed) is covered. Additionally, EPA uses a cutoff of 10^{-4} millimeters of mercury (mm Hg) for the vapor pressure of surrogates; any higher vapor pressure must be accounted for by considering the worker's perspective. Further volatility (e.g., 10^{-3} or 10^{-2} mm Hg) increases the exposure to both the aerosol measured in the studies and anything that is volatilizing. An examination would include the aerosol exposure as well as monitoring data or models to estimate the air concentration. The toxicity study itself also could be evaluated to determine whether vapor inhalation toxicity data were generated. Dr. Parkin thanked Mr. Leighton for his response.

Dr. George Fernandez observed that the diagram (Slide 8) shown by Mr. Jordan was meant to show proportionality, but there is a point that clearly shows there should be a nonlinear effect; studies usually show linear effects but not always.

Mr. Leighton clarified that when using surrogate data for a risk assessment, chemical-specific dermal absorption and toxicity information are considered.

Dr. William Popendorf commented that extrapolation in practice is said to be primarily from one chemical to another based on the concentration of the chemical in the product versus two products with the same concentrations. He wondered whether it happens that the amount one uses is substantially different between the two situations. Mr. Leighton replied that EPA considers both situations. For example, when homeowners use trigger spray pump pesticide products, what changes the AaiH is the concentration. A product with a 10-fold higher concentration might increase exposure. Dermal absorption of the chemical is another consideration. For someone in a hospital who uses much more product to clean operating rooms, the concentration would be the same but the volume would be much higher. In those instances, the volume would be indicated. It would have been useful to consider various concentrations (e.g., 0.2 to 20 percent) in the current study, but it would have required a separate study because it is not ethical to expose people to high concentrations of pesticides without chemical-resistant gloves or respiratory protection. That is one limitation to the design of this study, which will be discussed further.

Dr. José Manautou requested clarification that for concentrations over 20 percent, PPE would be required in exposure studies. Mr. Leighton responded that the ethical concentration cutoff is dependent on the chemical used. For example, quaternary ammonia compounds are irritants only at high concentrations greater than 10 to 20 percent.

Session 1: A completed study report from the AEATF in which the dermal and inhalation exposure of professional janitorial workers was monitored as they poured liquid antimicrobial pesticide products from conventional or reduced-splash containers into different sizes and types of receiving containers.

Background

Dr. Parkin introduced the AEATF study as one that the Board had reviewed in October 2011 and had a number of recommendations for the protocol. The Board is charged today to review the completed study and evaluate whether it met scientific and ethical expectations. Dr. Parkin asked Mr. Leighton to present the Agency's review of the scientific aspects of this study. Board members would then be provided an opportunity to ask clarifying questions.

EPA Science Assessment

Mr. Leighton welcomed the meeting participants. He remarked that this HSRB meeting was to be held on November 1, 2012, but was canceled because of Hurricane Sandy.
Mr. Leighton explained that the AEATF is comprised of 44 chemical companies that leverage

shared resources to accomplish the exposure studies mandated during the 2006 Science Advisory Panel (SAP) and 2007 HSRB meetings. EPA, Health Canada and Cal/EPA comprise a Joint Regulatory Committee (JRC) to review intentional human exposure studies. During the most recent convening of the Board in January 2012, the members had evaluated a completed AEATF study similar to the completed study on the agenda today.

Mr. Leighton presented EPA's review of the completed AEATF liquid pour study , which consisted of dermal and inhalation monitoring of workers pouring a liquid antimicrobial product from various size containers packaged in conventional and reduced-splash containers. Mr. Leighton explained that he would present EPA's science review, and Ms. Kelly Sherman (OPP, EPA) would present EPA's ethics review. Dr. Jonathan Cohen (ICF International), the contractor statistician integral to EPA's review efforts, was present by telephone to answer any questions.

Mr. Leighton noted that this fifth completed AEATF study was the most complex to date. He provided an overview of his presentation, which consisted of a description of the study, explanation of the AEATF's responsiveness to EPA and HSRB comments, outline of three main issues highlighted in EPA's science review, and conclusions. Mr. Leighton acknowledged that although the issues were challenging, the path forward to address each one was clear.

This liquid pour scenario was one of 17 AEATF scenarios, which also includes exposure studies evaluating mopping and the use of sprays and wipes, to evaluate antimicrobial products typically labeled for disinfectant use. The 17 scenarios originally were to be completed within 5 years, but that timeframe has been extended. The liquid pour study was completed indoors using two scenarios: conventional pour (CP) and reduced-splash (RS) containers. The product and receiving containers were of various sizes. For example, the receiving containers ranged from 2 gallons to 50 gallon troughs (e.g., for industrial applications). This study specifically monitored pouring events; the workers did not apply the treatment solution.

Although other studies occur in randomly selected buildings, a laboratory in Concord, Ohio, was selected for this study to reduce costs; this was not ruled to affect the overall use of the data. Monitoring was conducted in two rooms. Each subject was monitored once for CP and once for RS containers to produce two distinct monitoring sets. To ensure a diversity of individual exposures, one enrolled subject was assigned to each of six monitoring events (ME) in a group that was defined by the size of the product container for a total of three groups. There were 18 ME for CP and 18 for RS. The receiving container type, height (floor or chest-height) and use of a measuring cup also varied.

Dermal and inhalation exposure was monitored for six subjects in each of the three groups (18 total). CP containers contained didecyl dimethyl ammonium chloride (DDAC), while RS containers contained n-alkyl dimethyl benzyl ammonium chloride (ADBAC). This enabled the use of fewer test subjects to capture more information. Subjects wore inner whole-body dosimeters (WBD) as well as dosimeters outside of the clothing. No gloves were worn. Subjects wore Occupational Safety and Health Administration (OSHA) Versatile Sampler (OVS) tubes on their lapel to capture the breathing environment. Particle size was not measured.

Mr. Leighton presented a table (Slide 7) depicting the various MEs. He explained that although the original protocol had considered three separate groups, upon review of the results group 1 was divided into 1a and 1b to account for the differences of pouring into bottles. A CP container is similar in structure to a milk jug, while an RS container is engineered to reduce "glugging" through the addition of an extra spout. The inclusion of RS containers in the scenario was intended to determine whether engineering controls would decrease exposure and obviate some of the need for PPE. Product labels do not regulate the size of containers sold, so the researchers included a diversity of sizes in the study protocol, ranging from 24 ounces (oz) to 5 gallons, to represent what is available on the market. The subjects poured a specific number of product containers per ME (e.g., 10 containers poured per ME when the receiving container was 32 oz spray bottles or six 5 gallon buckets into the 50 gallon trough). Mr. Leighton reminded participants that the efforts of each individual subject could be found in Table 2 of the EPA Science Review and Tables 7 and 8 of the AEATF study report.

Mr. Leighton presented several photographs depicting the study scenario. The first photograph (Slide 8) showed a subject pouring from a gallon container into a measuring cup. The second photograph (Slide 9) illustrated a subject pouring liquid into a spray bottle with a visible spill down the bottle. Observational notes indicated that the spill contacted the subject's hand. Spills and drips happened frequently despite the professional janitorial background of the research subjects. This demonstrates that pouring liquid is not a highly trained skill, as spills happen even in a randomly selected janitorial population, and suggests that the data would be applicable to consumers as well as janitors. The next photograph (Slide 10) depicted a Group 2 ME where a subject poured from a 1 gallon container into a 4 gallon bucket at chest height. The remaining photographs (Slides 11-13) illustrated subjects pouring liquid into a trough with CP and RS containers. Prior to the study, investigators did not know whether RS would make a difference, so they were interested in looking at that variable.

The stated objective was for the liquid pour study to provide sample estimates of the arithmetic mean and 95th percentile of normalized exposure accurate to within three-fold, 95 percent of the time. Thus, the reviewers used a K-factor goal of three-fold relative accuracy in judging these data and sought an arithmetic mean that was within three times the lower and upper 95th confidence intervals.

Mr. Leighton described the responsiveness of the AEATF to EPA and HSRB comments. Prior to the HSRB evaluation, the JRC had worked with the AEATF to help submit the study to the HSRB. EPA and the HSRB then provided additional comments to improve the clarity and design of the study, recommending the inclusion of more random procedures and acknowledgement of design limitations (e.g., janitor versus consumer population, indoor versus outdoor). For example, there could be differences in the data if the study was performed outdoors. The AEATF responded to each specific comment to EPA's satisfaction.

Mr. Leighton lauded the AEATF for the few and minor protocol deviations, remarking that many deviations used to occur in these studies and there has been great improvement. Nine deviations were reported, including an uncalibrated bathroom scale, and there were no unreported deviations. EPA concluded that the deviations in the study do not affect the scientific validity of the use of the exposure results.

A diagram of a WBD was presented to demonstrate how the WBD could be sectioned to measure dermal exposure for a variety of clothing scenarios: long shirts/long pants (long-long), long pants/short shirts (long-short) and short shirts/short pants (short-short). After the ME, researchers removed the WBD and sectioned it into pieces; this provided another method to limit the subjects involved in the study.

Mr. Leighton explained that hand exposure was the primary driver in each exposure scenario. All laboratory and field blank samples were less than the limitation of quantitation (LOQ), and individual laboratory recoveries ranged from 75 to 116 percent. The field recoveries were used to correct dosimeters. Importantly, a stable surrogate chemical was chosen that would not be photo labile or otherwise degraded by laboratory conditions, which would result in underestimation of exposure. The mean recovery of all samples was approximately 90 to 100 percent, with four recovery samples falling outside of 70 to 120 percent (64, 67, 174 and 178 percent). The two highest values were not used to correct the field samples because there was a problem with the fortification. A 90 percent field sample recovery would mean that 10 percent was lost somewhere in the process, and a 10 percent correction would be applied the laboratory samples.

Subjects were instructed to work as they normally would to increase the random elements within the study. The mean amount of AaiH was 0.16 pounds (lb) for CP and 0.14 lb for RS containers. Mr. Leighton allowed that it would be interesting to have a wider range of AaiH within the protocol, but that was not possible given the need for PPE, specifically gloves, at higher levels of active ingredient. Most people pouring these liquids under normal circumstances do not use gloves. The time to pour varied by individual, with an average of 8 minutes for CP and 13 for RS containers. Subjects poured approximately 4 oz of liquid at a time into 10 to 15 bottles, or 30 gallons in 5 gallon increments.

Three methods were used to estimate unit exposures, including the empirical estimate, simple random sample (SRS) and mixed model. Empirical estimates are easy for people to understand and are presented in the docket, while the more complicated statistical models are contained within Tables 3 to 6 of the EPA Science Review. Following the 2006 SAP discussion, the mixed model was selected to best represent the unit exposure results. Mr. Leighton invited Dr. Cohen to give an explanation of the SRS versus mixed model results.

Dr. Cohen explained that all formulae were listed in Table 7 of EPA's Science Review and additional details could be found in Appendix A of EPA's Science Review. He remarked that for the empirical model, the geometric and arithmetic means were calculated separately for each group by taking the sum of exposures divided by the number of values. The geometric mean is the same for the simple lognormal model, but the arithmetic mean is calculated assuming a lognormal distribution, which includes multiplication by half of the variance. This results in a different estimated arithmetic mean than for the empirical model. Finally, the mixed model uses lognormal distribution but incorporates a random worker effect variable because the same worker tested CP and RS containers, which could occur in either order. It is likely that correlation exists between those two measurements, and the mixed model accounts for that

correlation. The geometric and arithmetic mean have different values, as does the geometric standard deviation.

Mr. Leighton remarked that the summary results of Table 1 in the EPA Science Review do not match Tables 3 through 6 because the calculations were performed using the mixed and empirical models. All models can be compared in the review's appendix.

Mr. Leighton highlighted three data issues identified by EPA. First, as already discussed, there were three rather than two distinct exposure scenarios. Second, the results were atypical for the clothing configurations, and third, there was an unexpected negative slope for dermal exposure.

Although the AEATF designed the liquid pour scenario to address two distinct exposure scenarios (CP and RS), after reviewing the results, EPA separated the results into three distinct exposure scenarios: bottle (i.e., using a spray bottle as a receiving container), CP into non-spray bottles and RS into non-spray bottles. This resulted in six MEs for Group 1a (bottle), which combined CP and RS events for the analysis. Other than bottles, the CP results were combined for all groups (15 MEs) and the RS results were combined for all groups (15 MEs). Mr. Leighton explained that these groups fell out logically and statistically after p values were calculated for various options. Grouping the bottles was logical because disinfectants often specify the use of spray bottles on the label, so the data from this scenario could be used specifically for spraying. The bottle group was a statistically justified unit exposure because the Groups 1a CP and 1a RS were not significantly different, while bottles compared to other receiving containers were significantly different for the two container choices. The p values of all combinations, as well as a summary of the statistics, are available within the EPA Science Review document.

The second issue addressed the fact that the results were atypical according to the clothing configurations. Each subject wore two WBDs, which were parsed into long-long, long-short and short-short configurations. This was done to account for the maximum exposure potential to a consumer, who might be wearing a short shirt and short pants. Janitors might wear a short shirt and long pants or a long shirt and long pants. Because the disinfectants are not irritants at low doses, there are no PPE requirements on the labels. The results were atypical in that more clothes resulted in a higher exposure; the unit exposure for the mixed model mean is greatest for the long-long configuration. The atypical results might be more understandable if a person were taking used gloves on and off, as they might get a higher exposure, but this did not occur. For CP container MEs, the mean was 10 for long-long, 9.9 for long-short, and 9 for short-short in units of milligrams (mg) per lb of active ingredient. Although these differences are small, the results are illogical and might result from a statistical quirk of the mixed model. Mr. Leighton emphasized that hand exposure accounts for the majority of the dermal exposure. Because of these atypical data, EPA will only consider the long-long configuration (the highest exposure data) when applying the results. Mr. Leighton referred participants to page 4 on the EPA Science Review for further explanation about these atypical results.

The third issue, Mr. Leighton explained, was the negative slope for dermal exposure. At the end of the January 2012 meeting, the Board members decided to explore options other than proportionality. The log-linear regression model postulates that the log of the exposure equals the

intercept plus the slope times the log of the AaiH plus error. If the slope equals 1, exposure is proportional to AaiH. If the slope is 0, exposure does not vary with AaiH, which is physically unrealistic because a worker is likely to spill some volume of the product on his or her hands, and a higher concentration of product would result in more exposure. If the slope is less than 0, this suggests that exposure decreases with AaiH, which also is unrealistic. Thus, the discussion about the volume poured and the concentration is relevant. The data in this scenario revealed a negative slope of -0.3 for the long-long configuration. As discussed, this is not a realistic result because pouring more product likely results in more spilling and thus a higher exposure. It is possible, however, that the random nature of spills accounts for the negative slope.

When EPA researchers saw these data, they first sought outliers as an explanation. Outliers would not be discarded, however, because the data represent someone using a pesticide as he or she usually would and spills occur in routine use. The slope did not change, however, even when outliers were removed. When the slopes were calculated separately for each scenario, all slopes remained negative. Although the inhalation data were more realistic, the data for dermal exposure showed a negative slope no matter how they were handled.

For the application of unit exposures, EPA will normalize the liquid pour data by AaiH. Logically, each drip or spill on the hands is a given volume of liquid and the exposure is dependent on the concentration of AaiH, which is calculated by the volume poured times the concentration. This relationship would be the same for residential use of pesticides as it would be for a hospital worker. Mr. Leighton explained that this approach is protective of human health. There are ways to characterize the limitations in the data using the threshold of AaiH to determine whether exposure will be under- or over-predicted. During the protocol evaluation stage, Dr. Michael Lebowitz had remarked that because people spill liquids, the AEATF might want to consider adding different concentrations to the protocol. Because of the need for chemical-resistant gloves when using higher concentrations, however, additional concentrations of AaiH were not included because a different scenario would have been required.

Mr. Leighton presented the unit exposures for the liquid pour scenario. The bottle subgroup displayed an arithmetic mean of 299 mg/lb active ingredient for dermal exposure (using long-long exposure data), while the CP and RS had much lower exposures of 10 and 3.1 mg/lb, respectively. Thus, the RS container lowered exposure by three-fold. With regard to inhalation exposure, the low vapor pressure of the chemical (10^{-6} to 10^{-8} mm Hg) meant that none of the samples were lost to volatility. The workers wore OVS tubes in the breathing zone to sample the full air environment. The samples could be normalized to mg/lb of active ingredient because sometimes there are oral endpoints without inhalation route-specific studies. This provides one method to do a route-to-route extrapolation, although the Agency is trying to move away from this. The results also show a time-weighted average of 8 hours, although any other time span could be calculated. The values are small because the pours are just 10 minutes long. Mr. Leighton noted that EPA did not have sufficient time to use values other than half of the quantification for the nondetected samples, so the values presented in EPA's Science Review are slightly different. When other multiple computation methods were applied to handle the nondetected samples after the HSRB review was postponed due to Hurricane Sandy, the bottle estimates decreased by 80 percent while the CP and RS scenarios increased by 10 or 20 percent. Approximately 40 percent of the samples were not detected.

To address the question of whether the sample was large enough, Mr. Leighton presented the K factors for each group. The three-fold relative accuracy goal was met for all three inhalation scenarios (bottle, CP and RS). For dermal exposures, the K value was less than three for CP and RS but not for the bottle, although the value was close (ranging from 3.1 to 3.6). EPA will use all of the results from this study at this point. The bottle results will be used because if the bottle results were to be combined with CP and RS, the disinfectant uses would be underestimated and all other uses would be overestimated. After all of the 17 planned AEATF studies are completed, there may be a need to refine the bottle unit exposure with additional monitoring. The current bottle results could be combined with CP and RS as designed, but logically it is better to separate those results.

The study design limitations were discussed previously during the protocol review of the HSRB and many are the same as those identified at the completion of the study. Study limitations include indoor versus outdoor use and janitor versus consumer use. The impact of pouring liquids indoor versus outdoor on exposures is unknown and would be expensive to determine. Most products are poured indoors. The exposure impact also is unknown for consumers versus janitors, but it is reasonable to use the data for both populations because as seen from the photographs, pouring liquids is not a highly skilled task and even professional janitors spill products.

Another design limitation is that the relative accuracy goal for the bottle scenario was not met. It is logical to use these data, however, because they are health protective. Normalizing dermal exposure by AaiH is another limitation. The threshold of AaiH characterizes when exposures are under- or over-predicting. It would have been useful to vary the concentration data, but this was not feasible. Another design limitation is that only the long-long clothing configuration data could be used. The amount of product that spilled on the subjects' hands was the driver of exposure. In the future, measuring only hand exposure is worth consideration to reduce study costs.

EPA plans to use the liquid pour study data generically to estimate the potential exposure to low- or moderate-volatility pesticides packaged as liquids for open pouring. Mr. Leighton explained that 10^{-4} mm Hg is low volatility. If a product has a higher volatility, exposure to aerosols will be a concern and the vapor phase would need to be accounted for or modeled separately. Disinfectant and sanitizer uses that include spray bottle type applications will use the bottle unit exposure scenario data. Mr. Leighton noted that the majority of assessments are performed using CP containers. The opportunity exists to reduce exposure if the industry adopts RS packaging; the JRC could support the use of RS containers.

In conclusion, EPA determined that the study results were sufficiently sound to support estimates of dermal and inhalation unit exposures. An adequate number of samples were collected for CP and RS; therefore, no additional MEs are required. Additional monitoring of the bottle scenario, however, might be warranted to refine the estimates. These data will be used now because the exposures are justified logically and statistically. EPA will know when to use the bottle estimate based on the label claims. EPA already recalculated the inhalation unit exposures using the multiple imputation method for nondetected samples. Importantly, data limitations

must be acknowledged in any assessments. Mr. Leighton offered to answer any questions regarding EPA's science review.

Board Questions of Clarification—Science

Dr. Parkin asked Board members if they required any clarifications. Dr. Dallas Johnson questioned whether the arithmetic mean resulted from transforming the lognormal mean back into the arithmetic mean. Mr. Leighton clarified that the arithmetic mean and 95th percentile were estimated from the results of the mixed model. The confidence intervals on each estimate relevant to the K factor are shown in Table 1 of the study review.

Dr. Linda Young asked which equation was used to calculate the maximum likelihood for substituting half-nondetects. Dr. Cohen explained that the equations were described in the appendix of the EPA Science Review. The investigators know that the values for inhalation exposure are between 0 and the detection limit. Dr. Young asked whether the EM algorithm was used because imputation depends on the parameters of the model, which in turn depend on the imputed value in an iterative process, and EM is one common method to use. Dr. Cohen explained that the calculation was performed by maximum likelihood in SAS, as SAS does not use the EM algorithm. He stated that the calculation is a similar algorithm, however, to find the maximum likelihood of the fitted model. Dr. Young mentioned that she saw imputation for 0 or one-half but did not see multiple imputation in the EPA Science Review models. She asked whether the SAS programming used PROC PMI. Dr. Cohen remarked that the program shows "percent macro impute." Where imputation occurred, the SAS mixed model and a nonlinear mixed procedure were used.

Dr. Young referenced three equations on page 36 of the appendix for her next question. Dr. Cohen confirmed that the "exposure equal" and "arithmetic mean exposure equal" were intended to follow the preceding line, and that the pounds of active ingredient would follow from those two equations. The arithmetic mean is the exposure given the amount of active ingredient. Dr. Young remarked that the equation was conditional on the pounds of active ingredient, which was not constant throughout the study.

Dr. Leonard Ritter noted that Mr. Leighton's presentation had indicated that two low and high values were rejected. Mr. Leighton clarified that only the two highest values were rejected because exposures are not corrected down if the whole average was above 100 percent. Dr. Ritter asked at what point when correcting for field recoveries are the data no longer trusted. Mr. Leighton responded that if two numbers were extreme, such as 0 percent and 200 percent that would indicate that the data should not be trusted. Precision also is important; if field recoveries were 28 to 34 percent and the coefficient of variation was good, the data would be used. Numbers are not discarded if they are precise. The surrogate choice is another consideration. If field recoveries show that only 30 percent of the sample is captured, the AEATF might pick a different surrogate. Compounds are selected that provide quality analytics and are not photo labile or otherwise susceptible to loss. Dr. Ritter remarked that the outliers might indicate that the surrogate is not the best fit in this instance.

Dr. Ritter asked how much of the exposure was driven by the hands relative to the remainder of the dermal exposure. Mr. Leighton responded that up to 98 percent of the exposure could be related to hand exposure. Dr. Ritter acknowledged that the effort and cost was significant to capture all dermal exposure. Hand exposure could be reduced by such efforts as wearing new gloves. Mr. Leighton mentioned that Board members had discussed whether just hands and inhalation should be monitored. The Pesticide Handler Exposure Database (PHED) also indicates that hands are a driver of exposure. This universal experience should be noted for future studies; resources previously allocated for dermal exposure could instead be applied to quality assurance and control.

Dr. Popendorf clarified that hands and face exposure were measured. He then asked whether any data existed regarding the use of spray bottles for janitors or custodians. Mr. Leighton answered that a consumer industry task force investigated which products are applied with what type of applicator (e.g., mop, aerosol can, trigger spray pump) and at what percentage. He remarked that the AEATF would be interested in investigating trigger spray pumps even if they were used 1 percent of the time. The information is available.

Dr. Popendorf remarked that the study subjects poured the liquid 10 to 15 times and wondered whether that happened in the real world. Mr. Leighton responded that hospital operating room custodians do pour liquids at that high of a volume. If only one bottle had been used per ME, dripping might have been missed. In response to a question, Mr. Leighton clarified that drips were not cleaned between pours, and no rag to clean the bottle was provided. Additionally, subjects were permitted to decide whether they would pour water or the product first into the container.

Dr. Popendorf referenced the comment in the report that stated that handling chemicals indoors resulted in a higher exposure than outdoors and asked for an elaboration. Mr. Leighton acknowledged that the statement was very broad and did not apply in such situations as when a liquid was poured outside and the air was blowing back into the handler's face.

Dr. Popendorf remarked that the report indicated that the air flow direction and subject orientation was to be monitored and questioned whether those data were included in the report. Mr. Leighton clarified that the laboratory was preset so the subjects could not change orientation. The researchers could help to clarify the direction in which the subjects were facing as they poured the liquids.

Dr. Popendorf acknowledged that all Board members agreed that concentration data could not be used at times. Because of the 40 percent of nondetect samples, he supported the monitoring of hands alone if there was a big enough spread of concentration. A 10-fold range might be enough, although three orders of magnitude would be preferable.

Dr. Sidney Green asked a question regarding the formulae for calculating unit exposure through the input of specific chemicals in relation to toxicologic endpoints of concern. Specifically, he was interested in how those studies would be conducted with the number of endpoints and dosages with each study. That information is not found in guidance documents. Mr. Leighton remarked that Dr. Green's question was outside of the scope of the science review,

but responded that regulatory authorities had the ability to use toxicity data, animal data, observational, and OSHA data that show when a sensory irritant elicits its peak effect. The exposure limit can be hit within a given timeframe. Dr. Green asked how the assessors decide which studies to use if limited to two to three dermal toxicity studies. Mr. Leighton responded that investigators choose between tier 1 and tier 2 toxicologic testing and 90-day oral and dermal studies. After consulting the database of studies, a committee of toxicologists collectively decides to take the lowest level of concern for uncertainty factors, which could result in a 100- or 1,000-fold uncertainty factor. The lowest level of concern from the group of studies, as well as other documents, determines how endpoints are selected.

Dr. Manautou questioned whether the sequence of pouring water and product was recorded for each subject. Mr. Leighton responded affirmatively and remarked that most subjects poured the product first. Dr. Manautou wondered whether the sequence might have affected the exposure. Later, Mr. Leighton clarified that all but one test subject poured the product before pouring the water. The one person who had begun pouring the water first switched the sequence during the ME.

Dr. Manautou asked whether spray bottles always were used for disinfectant purposes. Mr. Leighton responded that is not always the case, but usually a trigger spray pump is used for disinfectants. Newer labels indicate whether the product should be used with a mop, wipe or spray. Furthermore, the investigators did not know ahead of time that the results would be so different for the bottle MEs.

Dr. Parkin asked the Board whether they had any further questions or clarifications. Seeing that there were none, she asked Ms. Sherman for the Agency's ethics assessment.

EPA Ethics Assessment

Ms. Sherman stated that the AEATF protocol was reviewed by the HSRB in October 2011. The sponsors consented to address the HSRB comments and revised the protocol accordingly. The revised protocol was sent back to the approving Institutional Review Board (IRB) in January 2012, at which point recruiting and subject enrollment began. Monitoring occurred in February 2012, and the report was submitted to EPA in August 2012.

Subjects were recruited through advertisements in three local newspapers, including the *News-Herald* of Northern Ohio, the *Star Beacon* and *La Prensa* (a weekly bilingual English/Spanish publication). Most of the calls were in response to the advertisements in the *News Herald*. Interested callers were phone interviewed by an IRB-approved script to determine whether they met the inclusion criteria (e.g., prior janitorial experience, at least 18 years old, sufficient fitness to lift a 40-lb bucket). If the callers met the study criteria, they were scheduled for an informed consent meeting. Ms. Sherman explained that recruiting was consistent with the protocol, and the process was equitable and free of coercion or undue influence. In particular, placing the advertisements in various newspapers targeted different groups to minimize bias and achieve diversity.

The study director held initial consent meetings with small groups of potential subjects to explain the study procedures, describe inclusion and exclusion criteria, read the consent form, and answer questions. People were encouraged to ask questions and take the materials home to discuss with their friends and family. If a subject met the inclusion and exclusion criteria and was still interested in enrolling, he or she met one-on-one with the study director. Given that the subject was deemed to possess a good understanding of the materials, he or she was asked to sign the informed consent form (ICF) and was then considered a subject. Of the 22 people scheduled for one-on-one meetings with the study director, 20 were enrolled. One person decided not to move forward with the process, and another person was excluded because he or she was the spouse of someone who worked at the laboratory. Two people on the standby list went through the consent process, which brought the total to 22 enrolled. Ms. Sherman concluded that the consent process closely followed what was outlined in the protocol and was a good process. No deviations related to the consent process occurred.

Ms. Sherman described the subject demographics. Of the 18 subjects monitored, 15 were male and three were female. The mean age was 48 years. While all subjects possessed at least 1 year of janitorial experience, the mean years of experience was 12. All subjects preferred to speak in English.

When the subjects arrived at the study location, they were reminded about the details of the study and informed that they could withdraw at any time. Prior to dressing with the dosimeters, each subject was introduced to a medical professional (nurse or emergency medical technician) who examined the hands and face to ensure that no broken skin or sores existed to act as excluding factors. The three females self-administered a pregnancy test. After doing so, they were asked whether they still wanted to participate, and if they answered affirmatively, the study director confirmed that the test was negative. Researchers helped each subject put on the dosimeter, which was washed prior to use, as well as the air-sampling pump.

Ms. Sherman reminded the Board members that spillage occurred during the study, but this did not raise concern about the subjects' safety from an ethical standpoint because pouring liquid chemicals into bottles and troughs was a normal activity. There was no concern in terms of risk, and the study was conducted without noteworthy incident. None of the subjects felt sick or were injured during the monitoring. Subjects were told that they could take a break at any time and were given a break when switching from CP to RS containers, at which point they were offered a drink. In general, the conditions were undemanding. There was nothing ethically concerning in the notes taken by observers.

Ms. Sherman explained that in terms of responsiveness to the EPA and HSRB protocol reviews, the investigators did everything asked of them. Most of the Board's ethical qualms were related to improving the clarity of the ICF, and all of the changes were made.

The initial protocol was approved by the Independent Investigational Review Board, Inc. (IIRB) in August 2011. The study directors complied with all IIRB procedures and requirements in revising the protocol, which was approved by the IIRB in January 2012. Five amendments were approved by the IIRB, and five deviation reports were reviewed and acknowledged by the IIRB. None of the reported amendments or deviations was ethically significant and no

unreported deviations were found. One deviation involved the sequence of shoe removal. Originally, subjects were to remove their shoes after taking off the sampling pipe and hand wash, but this order was reversed to minimize contamination in the room. This deviation did not affect the ethics. The documentation of IIRB correspondence was complete and well-indexed. The requirements of 40 CFR §26.1303 for the documentation of ethical conduct were complete and satisfied.

Ms. Sherman concluded that the study met the substantive acceptance standards of 40 CFR §26.1703, 40 CFR §26.1705 and FIFRA §12(a)(2)(P). All subjects were at least 18 years old. There were no noteworthy deficiencies in the ethical conduct of the research, the protocol was faithfully executed as amended, and minor deviations did not compromise the safety of the subjects. Subjects were fully informed and consented to the study without coercion or undue influence.

In conclusion, Ms. Sherman reported that the available information indicates that the AEATF Liquid Pour Study was conducted in substantial compliance with subparts K and L of 40 CFR part 26.

Board Questions of Clarification—Ethics

Dr. Parkin solicited clarification questions from the Board members and none were proffered.

Public Comments

Dr. Parkin called for any public comments. Mr. Downing remarked that no public comments had been registered in advance. However, one member of the audience spoke up and wished to address a Board member's question from earlier in the meeting.

Dr. Leah Rosenheck (LR Risk Consulting, Inc.), the study director, addressed the comment from Dr. Popendorf regarding the orientation of workers with respect to the air flow. As suggested by the HSRB, the researchers did measure air flow within the two test rooms, and those measurements are contained within the report. The average air flow exchange ranged from 8 to 10 air exchanges per hour in room one and 7 air exchanges per hour in room two. A schematic on page 153 of the report shows the air flow and air vents with respect to the orientation of the workers. Dr. Rosenheck acknowledged that more detail regarding the workers' orientation could have been added to the report. She referred the Board members to photographs on page 156 of the report, which depicted the containers of chemicals that were placed on the ground or countertops. The pictures show that the workers were perpendicular to the air flow, facing the wall, when the containers were on the countertop. There was some movement of the workers, especially if they had to lift a container and then swivel to face the bucket to pour. Thus, the air flow was perpendicular, with the exception of the 5 gallon buckets because of the direction of the basins. In those MEs, the workers were parallel to the direction of the air flow.

Dr. Rosenheck elaborated on the question regarding the sequence of chemicals and water added to the spray bottles. Everyone added the chemical first and then the water. One person started by adding product to the bottle first, but had difficulty in stopping the water added to the

spray bottle before it overflowed. This subject then tried to add water to the spray bottle first but only did this once because he or she did not know how much water to add to leave room for the chemical product at the top. As this was inefficient, the subject reverted to adding the product first.

Dr. Manautou requested clarification from Dr. Rosenheck on the measurement cup that was used. He remarked that the measuring cup used in the first ME was not used in any subsequent MEs and noted that this was a modification. Dr. Rosenheck responded that originally the 8 oz measuring cup was to be used for Group 1 and the 16 oz cup for Group 2. The 8 oz measuring cup, however, did not have a spout. After the first ME, the researchers decided that all MEs should use the measuring cup with the spout. Dr. Manautou asked whether this resulted in a higher exposure for the first ME. Mr. Leighton answered that higher exposures were obtained within the study, so the data point was retained.

Dr. Manautou asked whether the subjects, all of which were janitors with at least 1 year of experience, had received safety training in their jobs. Previous experience might be indicative of safer handling of chemicals. Dr. Rosenheck acknowledged that all of the subjects had previous janitorial or property maintenance experience, but the investigators did not ask whether they had safety training or other formal training. She added that many of the subjects possessed more than 30 years of experience.

Dr. Popendorf questioned the frequency of typical liquid disinfectant use in the study population, as shown in Table 6 of the study report. Dr. Rosenheck responded that the participants were asked whether they pour liquid sanitizers as part of their job and how frequently, and most of the responses ranged from three times per week to daily.

Dr. Popendorf thanked Dr. Rosenheck for the diagram of the orientation of workers with respect to the air flow but deemed the volume of air exchanges per hour unhelpful. He asked whether information about the velocity of the air flow across the room existed. Dr. Rosenheck explained that the air flow measurements were taken to calculate the air exchange. Dr. Popendorf remarked that air flow typically is relative to room volume. Dr. Parkin concurred that the values would be dependent on the volume of the room. Dr. Rosenheck agreed to investigate what raw data were available, noting that the air flow calculations were not included in the report.
Dr. Popendorf asked whether the facilities had been renovated or otherwise modified in the year since the study. If nothing has changed, it might be possible to go back and conduct the air velocity measurements. Dr. Rosenheck agreed to confirm whether any changes had been made to the facility.

Dr. Popendorf asked Dr. Rosenheck about the statement in the AEATF report that declared broadly that indoor exposure was higher than outdoor exposure. Dr. Rosenheck commented that her experience with greenhouse studies indicated that indoor exposure tends to be higher. The PHED information appears to confirm that scenarios involving mixing and loading using a hand wand have higher dermal and inhalation exposure values for indoor than outdoor exposures. Dr. Rosenheck acknowledged that the statement would depend on the equipment in use and other factors, and Dr. Popendorf agreed.

Dr. Manautou asked where the water carboy was located relative to the dispensing containers. Dr. Rosenheck referred Dr. Manautou to page 157 of the report, which showed the spray bottles on the countertop near the containers. Dr. Manautou asked whether the distance remained consistent, and Dr. Rosenheck responded that the water carboys were used only with spray bottles and not in the other scenarios.

Dr. Parkin solicited any further questions for the lead investigator, and none were offered. She thanked Dr. Rosenheck for her answers.

Charge to the Board – Science

Ms. Sherman read the science charge questions into the record:

- Was the research reported in the AEATF completed liquid pour study report (AEA05) faithful to the design and objectives of the protocol and governing documents of the AEATF?

- Has EPA adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating the exposure of people who pour liquid antimicrobial pesticide products?

Board Science Review

Dr. Parkin asked Dr. Popendorf, as the lead discussant for the science review, to address the science charge questions. Dr. Popendorf agreed with the first charge question and the Agency's findings that the research reported in the AEATF completed liquid pour study was faithful to the design and objectives of the protocol and governing documents of the AEATF.

In response to the second charge question, Dr. Popendorf agreed broadly given several limitations. He presented several clarifying comments and a few modifications. He reiterated his concern with the experience of the workers given the variations detailed in the documented observations. For example, eight out of 18 subjects changed their handling process during the ME to reduce the amount of dripping that occurred. Clearly, prior experience is not a factor, but experience handling the product is a factor. These data parallel residential users more than Dr. Popendorf expected.

Another issue is that the handlers did not wipe the spills, and there was no time interval between each pouring event within the ME such that spills were not given time to dry. This suggests that the exposures were higher than expected for a typical use of once per day, which is the frequency reported by most of the subjects. Dr. Popendorf observed that the high exposure data is a positive finding.

Dr. Popendorf continued, remarking that there was not much justification for the statement that indoor exposure would be higher than performing the same activity outdoors. The study did not measure or document the velocity of the air drift. Although the air flow was probably sideways, ventilation might have been a factor, but the data are not available.

Dr. Popendorf restated EPA's declared limitation that the small sample size by itself does not create statistical limitations except for pouring into spray bottles. Dr. Popendorf remarked that the lack of variability in AaiH might have caused the odd statistics, not the fact that it was just six subjects in the group. He expressed concern with the lack of variability of the six people in the bottle group, which varied only by 1.3 in AaiH. The other groups (CP and RS) varied by four- to seven-fold in AaiH.

Another point of discussion was the issue of concentration. The Agency justifies the use of unit exposure values to adjust for concentration, but in this case all of the concentrations were the same and the only variation was the volume used. The fact that the statistics were weak should not be taken as evidence of weakness of applicability of unit exposure to extrapolate values on the basis of concentrations, which is strong. There is an implicit assumption that the volume used times the rate of exposure while in use has to be similar because the volume is expected to correlate with exposure. If the rate of exposure changed, exposure could increase or decrease. Eight out of 18 subjects changed their behavior, which is another strong case for why the data need not be expected to follow proportionality. Dr. Popendorf indicated that the study data provide good justification to reduce the concentration 10-fold, even 100-fold, to try to get better power and achieve proportionality solely with hand exposure.

Dr. Popendorf also remarked on the difference in the relatively low aerosol generation between the CP and RS scenarios. The T-test showed a difference with a 0.01 significance level. There are good reasons to pour from containers that have engineering controls. The respiratory volume per minute rate used by the EPA in the science review was 1 cubic meter per hour (m^3/hr), but several guidance documents should be considered, including the Occupational and Residential Exposure Test Guidelines, which suggest a different value of 1.33 m^3/hr.

Dr. Parkin asked Dr. Popendorf for his official response to the second science charge question, to which he replied that EPA had not adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating the exposure of people who pour liquid antimicrobial pesticide products, but they could do so in the future.

Dr. Parkin asked Dr. Young, the associate discussant for the science review, to present her comments. Dr. Young declared that the answer to the first question was "yes," and the answer to the second question was "not yet," but more could be done. She explained her comments from a statistical point of view. First, the method of imputation used for the multiple imputation is incorrect because there might be reasons explaining the big changes in numbers. The problem lies with the initial estimate parameters used to generate the imputation values. Estimate parameters will change, which means that the imputed values are no longer correct for the estimated parameters. It is important to conduct this iterative process until the estimates do not vary. If multiple imputation is to be performed, it needs to be an iterative process so the imputed effects are consistent with the parameters. A five-fold imputation is the standard approach to capture variation. Means do not vary as much as individual values; imputing five values would take advantage of the variation in the five values rather than imputing the average. Bayesian analysis is not required; there is a SAS procedure to perform multiple imputation analysis.

Dr. Young reiterated Dr. Johnson's remark questioning the value of the arithmetic mean. The problem is illustrated on page 36 of Appendix A, which shows the constant as the arithmetic mean of the exponentiation of the intercept times the exponentiation of the error term. That becomes a constant, however, only if the AaiH does not vary and the slope is 1. The equation is invalid and the arithmetic mean of exposure is incorrect, as all three of the HSRB statisticians agreed. When exposure is considered, the intercept is a constant but the pounds of active ingredient and the error term depends on the observation, which cannot be separated. This equation could be improved with a Taylor series expansion, but that has its own problems. The error term being used is a mixed model with two variance components—one for the worker and one for the air environment—which cannot be combined. All of this is predicated on the fact that the geometric mean falls out naturally but EPA wants an arithmetic mean. Dr. Young opined that there is no great value in calculating the arithmetic mean; calculating confidence intervals on the geometric mean would be more valuable.

Dr. Young also questioned the Q-Q plots. The assumption is a constant mean between the three groups (bottle, CP and RS). Given that the mean is different for each group, the researchers should use the residuals and not the observed values for each container type in the Q-Q plots to assess how the results could be improved. The residual of the model and the worker need to be separated to be evaluated appropriately in the Q-Q plot.

Dr. Young also expressed concern with the variance among the groups, which were not the same. She did not see the model account for the differences in variance within the SAS code. The study does not have a random sample. It would be useful to consider the inequality in the variances within the model before discarding that variable. The differences in the groups, variance, and repeated measures for the same worker must be accounted for because it is not a simple random sample.

Dr. Young remarked that the slope of the equation causes issues. The Board needs to decide how they will react if they receive results indicating a slope greater than 1. If the estimated slope is between 0 and 1, the HSRB can argue that it is protective of human health, but this argument is not valid for values greater than 1. Negative estimated slopes do not make any sense. Slopes of zero also are not realistic, but EPA either must entertain the fact that the slope is 0 or separate the hands into a discrete analysis, which might show a slope of 1.

Dr. Young declared that great progress had been made, but the present analysis contains severe, but fixable, limitations to the data as analyzed.

Dr. Parkin expressed appreciation to Dr. Young for her analysis and offered Dr. Manautou, the other associate discussant, an opportunity to speak. Dr. Manautou agreed with the points of clarification identified and expressed interest in a more detailed explanation for how the third exposure group was generated in terms of a statistical justification. In particular, he questioned how two factors are related statistically when they are interconnected. Mr. Leighton referred Dr. Manautou to Table 8 (in Appendix A of the EPA Science Review) for a more thorough statistical review and an explanation as to what provides more justification when deciding to separate the groups, the statistics or the logic. He emphasized that the logic would need to exist to justify separating the groups. Dr. Manautou requested clarification for the over- versus underestimation of exposure. Mr. Leighton responded that the two scenarios were first evaluated as

designed and the combined exposures were higher than the CP (10 mg/lb) but lower than the bottle values (299 mg/lb). He emphasized that EPA had looked at the two scenarios of the study as designed before deciding to separate the bottle events.

Dr. Parkin requested any additional discussion by Board members. Dr. Kissel noted that the thresholds for under- and overestimation occur for two-thirds of the scenarios (CP and RS) at approximately 1,000 oz of product and at 30 oz for the bottle. Application of that volume of product to achieve the threshold of active ingredient exceeds what would be expected for 1 day of domestic use. He asked whether EPA, as it moved forward and used these data in models for domestic exposure, planned to acknowledge that these data might lead to an underestimation of exposure. Mr. Leighton remarked that EPA looks at the requirements of the label, such as the percentage of active ingredient. If the values were underestimated, more data would need to be collected. He clarified that domestic use was equivalent to consumer or nonoccupational use.

Dr. Jordan explained that products sold for disinfectant use with trigger spray pumps were marketed differently, not labeled differently. When assessing the risk of the product, researchers would assess exposures associated with the assumption that the product would be used repeatedly by the same person in multiple locations (e.g., multiple bathrooms in a hotel). Mr. Leighton remarked that one should look at the high end for exposure to a product. Problems occur if the values fall below the threshold. Dr. Kissel remarked that standard operating procedures (SOP) must be written very carefully because a potential misinterpretation of the label could lead to misuse of the product.

Dr. Kissel elaborated that the question relevant to the indoor and outdoor exposure issue involved aerosolization. One psychological factor that might affect exposure is that workers might be more careful and more inclined to clean spills that happen inside. If the worker is pouring a liquid outside, they might be less careful and might end up with product on their pant legs, for example. Thus, the indoor versus outdoor exposure argument extends beyond aerosols, and behavior should be considered in deciding whether indoor or outdoor exposures would be equivalent.

Dr. Kissel agreed with the proposition that hand exposures should not be combined with the other dermal exposures, given the disparity in values between hand and other dermal exposures. The dermal exposures might comprise a fixed fractional absorption that is unrelated to the loading. Dr. Kissel remarked that bad science is unethical. The exposure load on the hands might be so high that uptake is inefficient, and people wash their hands more frequently. If product ends up on the pant leg, the exposure load will be low but it might be absorbed efficiently. Dr. Kissel expressed support for investigating the exposure to hands separately from the rest of the body given the logic of the situation.

Dr. Popendorf offered a consensus response. In response to the first charge question, all answers have been “yes.” In response to the second charge question, the answer is “yes,” with some qualifications.

Dr. Parkin asked the Board members if anyone dissented to the affirmative answer to question one, and no one did. There also was no dissent for the second question being answered "yes, but."

Charge to the Board – Ethics

Ms. Sherman read the ethics charge question into the record:

- Does the available information support a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR part 26?

Board Ethics Review

Dr. Parkin asked lead discussant Dr. Virginia Ashby Sharpe to comment on the ethics review. Dr. Sharpe expressed appreciation to the lead investigator for being so responsive to the Board's comments during the proposal review and making the completed proposal review so easy. She also thanked Ms. Sherman for her ethics review, which included a decisive and detailed evaluation of the proposal and results. Dr. Sharpe presented her and Dr. Halanych's conclusions, which indicated that the available information supports a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR part 26. Dr. Halanych verbally confirmed Dr. Sharpe's conclusions.

Dr. Parkin solicited any ethical issues or concerns from the Board members. There being none, she asked Dr. Sharpe to repeat the specific response to the charge question. Dr. Sharpe replied that the available information supports a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR part 26. Dr. Parkin asked the Board members whether there was any dissent with regard to the ethics charge question or any remaining key issues to discuss. As none of the Board members disagreed with the charge question responses, Dr. Parkin remarked that the HSRB had completed its responses to the charge questions.

An Update from the Work Group on the Return of Individual Research Results

Dr. Parkin acknowledged that the HSRB had convened a work group to investigate the return of research results to participants in third-party studies. The work group, which consists of HSRB members as well as external experts, met for a full day of deliberations on January 16, 2013. The work group is expected to report to the HSRB in 2013 for a public debate after securing a committee-wide agreement on how best to proceed with the return of individual research results, which is a topic that arose during several HSRB discussions in recent years.

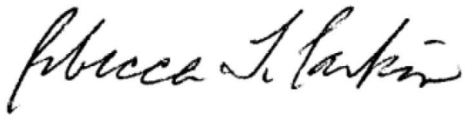
Adjournment

Dr. Parkin expressed appreciation to the Board members for their diligent work during this review. Mr. Downing thanked the Board members for their productive discussion. He explained that the next HSRB meeting is scheduled for April 8 to 12, 2013. A notice of the exact dates and times will be issued in the *Federal Register* and on the HSRB website. Mr. Downing adjourned the meeting at 4:33 p.m.

Respectfully submitted:

Jim Downing
Designated Federal Officer
Human Studies Review Board
United States Environmental Protection Agency

Certified as accurate:



Rebecca T. Parkin, Ph.D., M.P.H.
Chair
Human Studies Review Board
United States Environmental Protection Agency

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by Board members during the course of deliberations within the meeting. Such ideas, suggestions and deliberations do not necessarily reflect definitive consensus advice from the Board members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final report prepared and transmitted to the EPA Science Advisor following the public meeting.

Attachments

Attachment A	EPA HSRB Members
Attachment B	*Federal Register* Notice Announcing Meeting
Attachment C	Public Meeting Agenda

Attachment A

EPA HUMAN STUDIES REVIEW BOARD MEMBERS

Chair

+Rebecca Tyrrell Parkin, Ph.D., M.P.H. Term: 10/1/07-8/31/2013
Professorial Lecturer (EOH)
School of Public Health and Health Services
The George Washington University
Lake Frederick, VA

Vice Chair

+Jewell H. Halanych, M.D. Term: 11/14/11-8/31/2014
Assistant Professor
Department of Medicine
Division of Preventative Medicine
University of Alabama at Birmingham
Birmingham, AL

Members

+George C.J. Fernandez, Ph.D. Term: 5/1/2010-8/31/2013
Statistical Training Specialist
SAS Institute, Statistical Training and Technical Services
Sparks, NV

+Sidney Green, Jr., Ph.D., Fellow, ATS Term: 10/19/2009-8/31/2015
Department of Pharmacology
Howard University College of Medicine (Retired)
Silver Spring, MD

+Elizabeth Heitman, Ph.D. Term: 9/1/2012-8/31/2015
Associate Professor of Medical Bioethics
Center for Biomedical Bioethics and Society
Vanderbilt University Medical Center
Nashville, TN

+Dallas E. Johnson, Ph.D. Term: 8/31/2007-8/31/2013
Professor Emeritus
Department of Statistics
Kansas State University
Manhattan, KS

+John C. Kissel, Ph.D. Term: 9/1/2012-8/31/2015
Department of Environmental
and Occupational Health Sciences
School of Public Health
University of Washington
Seattle, WA

+José E. Manautou, Ph.D. Term: 5/1/2010-8/31/2013
Associate Professor of Toxicology
Department of Pharmaceutical Sciences
School of Pharmacy
University of Connecticut
Storrs, CT

+William J. Popendorf, Ph.D. Term: 10/19/2009-8/31/2015
Professor Emeritus
Department of Biology
Utah State University
Logan, UT

^Nu-May Ruby Reed, Ph.D., D.A.B.T. (1992-2012) Term: 9/1/2012-8/31/2015
Retired Staff Toxicologist
California Environmental Protection Agency (Cal/EPA)
Department of Pesticide Regulation
Davis, CA

+Leonard Ritter, Ph.D., ATS Term: 11/14/2011-8/31/2014
Professor Emeritus (Toxicology)
School of Environmental Sciences
University of Guelph
Guelph, ON, Canada

+Virginia Ashby Sharpe, Ph.D. Term: 5/1/2010-8/31/2013
National Center for Bioethics in Health Care
Veterans Health Administration
Department of Veterans Affairs
Washington, DC 20420

Bernard A. Schwetz, D.V.M., Ph.D. Term: 11/14/2011-8/31/2014
Retired Director
Office of Human Research Protections
Department of Health and Human Services
Cadott, WI

+Linda J. Young, Ph.D. Term: 3/28/2008-8/31/2014
Professor and Associate Chair
Department of Statistics
Institute of Food and Agricultural Sciences
University of Florida
Gainesville, FL

+Present on January 17, 2013
^Present via telephone January 17, 2013

Attachment B

Federal Register Notice Announcing Meeting

[*Federal Register* Volume 77, Number 239 (Wednesday, December 12, 2012)]
[Notices]
[Pages 74004 -74006]
From the *Federal Register Online* via the Government Printing Office [www.gpo.gov]
[FR Doc No: 2012-29983]

ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-ORD-2012-0892; FRL-9761-4]

Human Studies Review Board (HSRB); Notification of a Public Meeting

AGENCY: U.S. Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The EPA Office of the Science Advisor announces a public meeting of the Human Studies Review Board to advise the Agency on the EPA scientific and ethical reviews of research with human subjects

DATES: This public meeting will be held on January 17, 2013, from approximately 1:00 p.m. to approximately 4:30 p.m. Eastern Time. Comments may be submitted on or before noon (Eastern Time) on Thursday, January 10, 2013

ADDRESSES: Submit your written comments, identified by Docket ID No. EPA-HQ-ORD-2012-0982, by one of the following methods:

Internet: http://www.regulations.gov: Follow the on-line instructions for submitting comments.

E-mail: ORD.Docket@epa.gov.

Mail: Environmental Protection Agency, EPA Docket Center (EPA/DC), ORD Docket, Mailcode: 28221T, 1200 Pennsylvania Avenue, NW, Washington, DC 20460.

Hand Delivery: The EPA/DC Public Reading Room is located in the EPA Headquarters Library, Room Number 3334 in the EPA West Building, located at 1301 Constitution Avenue, NW, Washington, DC 20460. The hours of operation are 8:30 a.m. to 4:30 p.m. Eastern Time, Monday through Friday, excluding Federal holidays. Please call (202) 566-1744 or e-mail the ORD Docket at ord.docket@epa.gov for instructions. Updates to Public Reading Room access are available on the Web site (http://www.epa.gov/epahome/dockets.htm).

Instructions: Direct your comments to Docket ID No. EPA-HQ-ORD- 2012-0892. EPA's policy is that all comments received will be included in the public docket without change and may be made available online at http://www.regulations.gov, including any personal information provided, unless the comment includes information claimed to be Confidential Business

Information (CBI) or other information the disclosure of which is restricted by statute. Do not submit information that you consider to be CBI or otherwise protected through http://www.regulations.gov or e-mail. The http://www.regulations.gov Web site is an "anonymous access" system, which means EPA will not know your identity or contact information unless you provide it in the body of your comment. If you send an e-mail comment directly to EPA without going through http://www.regulations.gov, your e-mail address will be automatically captured and included as part of the comment that is placed in the public docket and made available on the Internet. If you submit an electronic comment, EPA recommends that you include your name and other contact information in the body of your comment and with any electronic storage media you submit. If EPA cannot read your comment due to technical difficulties and cannot contact you for clarification, EPA may not be able to consider your comment. Electronic files should avoid the use of special characters, any form of encryption, and be free of any defects or viruses.

FOR FURTHER INFORMATION CONTACT: Any member of the public who wishes to receive further information should contact Jim Downing at telephone number: (202) 564-2468; fax: (202) 564-2070; e-mail address: downing.jim@epa.gov, or Lu-Ann Kleibacker at telephone number: (202) 564-7189; fax: 202-564-2070; e-mail address: kleibacker.lu-ann@epa.gov; mailing address: Environmental Protection Agency, Office of the Science Advisor (8105R), 1200 Pennsylvania Avenue, NW, Washington, DC 20460. General information concerning the EPA HSRB can be found on the EPA Web site at http://www.epa.gov/osa/hsrb/.

SUPPLEMENTARY INFORMATION:

Location: The meeting will be held at the Environmental Protection Agency, Conference Center—Lobby Level, One Potomac Yard (South Building.) 2777 S. Crystal Drive, Arlington, VA 22202.

Meeting access: Seating at the meeting will be on a first-come basis. To request accommodation of a disability, please contact the persons listed under **FOR FURTHER INFORMATION CONTACT** at least ten business days prior to the meeting using the information under **FOR FURTHER INFORMATION CONTACT**, so that appropriate arrangements can be made.

Procedures for providing public input: Interested members of the public may submit relevant written or oral comments for the HSRB to consider during the advisory process. Additional information concerning submission of relevant written or oral comments is provided in Section I, "Public Meeting," under subsection D. "How May I Participate in this Meeting?'" of this notice.

I. Public Meeting

A. Does this action apply to me?

This action is directed to the public in general. This action may, however, be of particular interest to persons who conduct or assess human studies, especially studies on substances regulated by EPA, or to persons who are, or may be required to conduct testing of chemical substances under the Federal Food, Drug, and Cosmetic Act (FFDCA)

[[Page 74005]]

or the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). This notice might also be of special interest to participants of studies involving human subjects, or representatives of study

participants or experts on community engagement. Since many entities may also be interested, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the applicability of this action to a particular entity, consult Jim Downing or Lu-Ann Kleibacker listed under **FOR FURTHER INFORMATION CONTACT**.

B. How can I access electronic copies of this document and other related information?

In addition to using regulations.gov, you may access this Federal Register document electronically through the EPA Internet under the "Federal Register" listings at http://www.epa.gov/fedrgstr/.

Docket: All documents in the docket are listed in the http://www.regulations.gov index. Although listed in the index, some information is not publicly available, e.g., CBI or other information whose disclosure is restricted by statute. Certain other material, such as copyrighted material, will be publicly available only in hard copy. Publicly available docket materials are available either electronically in http://www.regulations.gov or in hard copy at the ORD Docket, EPA/ DC, Public Reading Room. The EPA/DC Public Reading Room is located in the EPA Headquarters Library, Room Number 3334 in the EPA West Building, located at 1301 Constitution Avenue, NW, Washington, DC 20460. The hours of operation are 8:30 am to 4:30 p.m. Eastern Time, Monday through Friday, excluding Federal holidays. Please call (202) 566-1744 or email the ORD Docket at ord.docket@epa.gov for instructions. Updates to Public Reading Room access are available on the Web site (http://www.epa.gov/epahome/dockets.htm).

EPA's position paper(s), charge/questions to the HSRB, and the meeting agenda will be available by the first of January 2012. In addition, the Agency may provide additional background documents as the materials become available. You may obtain electronic copies of these documents, and certain other related documents that might be available electronically, from the regulations.gov Web site and the EPA HSRB Web site at http://www.epa.gov/osa/hsrb/. For questions on document availability, or if you do not have access to the Internet, consult either Jim Downing or Lu-Ann Kleibacker listed under **FOR FURTHER INFORMATION CONTACT**.

C. What should I consider as I prepare my comments for EPA?

You may find the following suggestions helpful for preparing your comments:

1. Explain your views as clearly as possible.
2. Describe any assumptions that you used.
3. Provide copies of any technical information and/or data that you used to support your views.
4. Provide specific examples to illustrate your concerns and suggest alternatives.
5. To ensure proper receipt by EPA, be sure to identify the docket ID number assigned to this action in the subject line on the first page of your response. You may also provide the name, date, and Federal Register citation.

D. How may I participate in this meeting?

You may participate in this meeting by following the instructions in this section. To ensure proper receipt by EPA, it is imperative that you identify docket ID number EPA-HQ-ORD-2011-0954 in the subject line on the first page of your request.

1. Oral comments. Requests to present oral comments will be accepted up to Thursday, January 19, 2012. To the extent that time permits, interested persons who have not pre-registered may be permitted by the Chair of the HSRB to present oral comments at the meeting. Each individual or group wishing to make brief oral comments to the HSRB is strongly advised to submit their

request (preferably via e-mail) to Jim Downing or Lu-Ann Kleibacker, under **FOR FURTHER INFORMATION CONTACT**, no later than noon, Eastern Time, Thursday, January 19, 2012, in order to be included on the meeting agenda and to provide sufficient time for the HSRB Chair and HSRB Designated Federal Official (DFO) to review the meeting agenda to provide an appropriate public comment period. The request should identify the name of the individual making the presentation and the organization (if any) the individual will represent. Oral comments before the HSRB are generally limited to five minutes per individual or organization. Please note that this includes all individuals appearing either as part of, or on behalf of, an organization. While it is our intent to hear a full range of oral comments on the science and ethics issues under discussion, it is not our intent to permit organizations to expand the time limitations by having numerous individuals sign up separately to speak on their behalf. If additional time is available, further public comments may be possible.

2. Written comments. Submit your written comments prior to the meeting. For the HSRB to have the best opportunity to review and consider your comments as it deliberates on its report, you should submit your comments at least five business days prior to the beginning of this meeting. If you submit comments after this date, those comments will be provided to the Board members, but you should recognize that the Board members may not have adequate time to consider those comments prior to making a decision. Thus, if you plan to submit written comments, the Agency strongly encourages you to submit such comments no later than noon, Eastern Time, Thursday, January 19, 2012. You should submit your comments using the instructions in Section I., under subsection C., "What should I consider as I prepare my comments for EPA?" In addition, the Agency also requests that persons submitting comments directly to the docket also provide a copy of their comments to Jim Downing or Lu-Ann Kleibacker listed under **FOR FURTHER INFORMATION CONTACT**. There is no limit on the length of written comments for consideration by the HSRB.

E. Background

The HSRB is a Federal advisory committee operating in accordance with the Federal Advisory Committee Act (FACA) 5 U.S.C. App.2 Sec.9. The HSRB provides advice, information, and recommendations to EPA on issues related to scientific and ethical aspects of human subjects research. The major objectives of the HSRB are to provide advice and recommendations on: (1) Research proposals and protocols; (2) reports of completed research with human subjects; and (3) how to strengthen EPA's programs for protection of human subjects of research. The HSRB reports to the EPA Administrator through EPA's Science Advisor.

1. Topics for discussion. At its meeting on January 17, 2013, EPA's Human Studies Review Board will consider scientific and ethical issues surrounding these topics:

a. A completed study report from the Antimicrobial Exposure Assessment Task Force II (AEATF) in which the dermal and inhalation exposure of professional janitorial workers was

[[Page 74006]]

monitored as they poured liquid antimicrobial pesticide products from conventional or reduced-splash containers into different sizes and types of source containers. EPA seeks the advice of the HSRB on the scientific soundness of this completed research and on its appropriateness for use in estimating exposure that results from pouring liquid antimicrobial pesticide products. EPA also seeks the advice of the HSRB on whether available information supports a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR Part 26.

2. Meeting minutes and reports. Minutes of the meeting, summarizing the matters discussed and recommendations, if any, made by the advisory committee regarding such matters, will be released within 90 calendar days of the meeting. Such minutes will be available at http://www.epa.gov/osa/hsrb/ and http://www.regulations.gov. In addition, information regarding the Board's Final meeting report, will be found at http://www.epa.gov/osa/hsrb/ or from the person listed under **FOR FURTHER INFORMATION CONTACT**.

Dated: December 3, 2012.

Glenn Paulson

EPA Science Advisor

[FR Doc. 2012-29983 Filed 12-11-12; 8:45 am]
BILLING CODE 6560-50-P

Attachment C

U.S. ENVIRONMENTAL PROTECTION AGENCY (EPA)
HUMAN STUDIES REVIEW BOARD (HSRB)
JANUARY 2013 PUBLIC MEETING AGENDA

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

Thursday, January 17, 2013

HSRB WEB SITE http://www.epa.gov/osa/hsrb/
Docket Telephone: (202) 566 1752
Docket Number: EPA–HQ–ORD–2012–0892

1:00 PM* **Convene Public Meeting** – Mr. Jim Downing, Designated Federal Officer, EPA HSRB, Office of the Science Advisor (OSA)
Introduction of Board Members – Dr. Rebecca Parkin, Ph.D., MPH, HSRB Chair
Welcome – Dr. Glenn Paulson, Ph.D., Science Advisor, EPA

Opening Remarks – Dr. Steven Bradbury, Ph.D., Director, Office of Pesticide Programs (OPP), Office of Chemical Safety and Pollution Prevention (OCSPP), EPA
Follow-Up on Previous HSRB Recommendations – Mr. William Jordan, OPP, OCSPP, EPA

Session 1: **A completed study report from the Antimicrobial Exposure Assessment Task Force II (AEATF) in which the dermal and inhalation exposure of professional janitorial workers was monitored as they poured liquid antimicrobial pesticide products from conventional or reduced-splash containers into different sizes and types of receiving containers.** EPA seeks the advice of the HSRB on the scientific soundness of this completed research and on its appropriateness for use in estimating exposure that results from pouring liquid antimicrobial pesticide products. EPA also seeks the advice of the HSRB on whether available information supports a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR Part 26.

1:40 PM **EPA Science Review** – Mr. Tim Leighton (OPP, EPA), Dr. Jonathan Cohen, Ph.D. (ICF International)
2:15 PM **Board Questions of Clarification** – Dr. Rebecca Parkin, Ph.D., MPH (HSRB Chair), EPA, Principal Investigator/Sponsor
2:45 PM **EPA Ethics Assessment** – Ms. Kelly Sherman (OPP, EPA)
3:15 PM **Board Questions of Clarification** – Dr. Rebecca Parkin, Ph.D., MPH (HSRB Chair), EPA, Principal Investigator/Sponsor
3:45 PM **Break**
3:55 PM **Public Comments**

4:05 PM Board Discussion

Charge to the Board – Science:

- Was the research reported in the Antimicrobial Exposure Assessment Task Force II (AEATF) completed liquid pour study report (AEA05) faithful to the design and objectives of the protocol and governing documents of AEATF?

- Has EPA adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating the exposure of people who pour liquid antimicrobial pesticide products?

Charge to the Board – Ethics:

- Does the available information support a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR Part 26?

5:00 PM* Adjournment

*Agenda times are approximate and subject to change depending upon the discussion.