Minutes of the
United States Environmental Protection Agency (EPA)
Human Studies Review Board (HSRB)
January 26, 2012 Public Meeting
Docket Number: EPA-HQ-ORD-2011-0954
HSRB Website: http://www.epa.gov/osa/hsrb

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

Date and Time:	Thursday, January 26, 2012, 9:45 AM – 4:30 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:	Sean Philpott, Ph.D., M.S. Bioethics
	Vice Chair:	Rebecca T. Parkin, Ph.D., M.P.H.
	Board Members:	Janice Chambers, Ph.D., D.A.B.T. George C.J. Fernandez, Ph.D. Sidney Green, Jr., Ph.D., Fellow, ATS Jewell H. Halanych, M.D. Dallas E. Johnson, Ph.D. Michael D. Lebowitz, Ph.D., FCCP (via telephone) Jerry A. Menikoff, M.D. William J. Popendorf, Ph.D. 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 9:45 a.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 Board 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 were two interesting and challenging topics on the agenda for the meeting. He noted that agenda times are approximate, with the exception that the afternoon session will start at 1:30 p.m. due to the availability of a Board member. Following the presentations, time has been scheduled for questions of clarification to EPA staff and the principal investigator and sponsors of the studies discussed. 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 two topics under consideration. 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-2011-0954 and most are available on the HSRB website at http://www.epa.gov/osa/hsrb. 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 the Board review and subsequent approval of the report in the Federal Register. Mr. Downing turned the meeting over to the HSRB Chair, Dr. Sean Philpott.

Introduction and Identification of Board Members

Dr. Philpott noted that the Board worked on a consensus model, and that consensus opinions of the Board would be included in the final report. He asked Board members to introduce themselves, and members completed their introductions. Dr. Philpott invited Dr. Warren Lux (Director, Program in Human Research Ethics, OSA, EPA) to offer welcoming remarks.

Welcoming Remarks

Dr. Lux welcomed all in attendance to the first face-to-face HSRB meeting of 2012. He extended a special welcome to the four original Board members whose terms are nearing completion, Dr. Philpott, Dr. Janice Chambers, Dr. Michael Lebowitz and Dr. Jerry Menikoff. Dr. Lux explained that those four members have helped to shape the Board into the thriving institution it is recognized as now since its inception as an untested entity in 2006. The Board has acquired credibility and stature that complement its success, to the benefit of the Agency, stakeholders and research colleagues. The projected agenda for 2012 raises the possibility that there will be no new agenda topics for the Board to review until October. If that is the case, Drs. Philpott, Chambers, Lebowitz and Menikoff will have completed their HSRB tenure. With the prospect of this meeting being their final meeting on the HSRB, Dr. Lux thanked the departing Board members for their service personally and on behalf of the Agency.

Office of Pesticide Programs (OPP) Follow-Up on Previous HSRB Recommendations

Dr. Philpott welcomed Mr. William Jordan (OPP, EPA) to give the follow-up of the previous recommendations. Mr. Jordan proffered greetings and expressed appreciation for the efforts of the Board on behalf of Dr. Steven Bradbury (Director, OPP, EPA). Mr. Jordan reiterated Dr. Lux's appreciation for the four departing Board members and commended their extraordinary amount of work and commitment throughout all 22 HSRB meetings. He thanked Drs. Philpott, Chambers, Lebowitz and Menikoff for their thorough and thoughtful reviews, and noted that they have made a real difference in the quality of research in terms of science and ethics. Mr. Jordan thanked all of the Board members for their public service.

Mr. Jordan discussed four topics reviewed by the Board at the previous HSRB meeting. The Antimicrobial Exposure Assessment Task Force (AEATF) protocol discussed previously was designed to evaluate the dermal and inhalation exposure resulting from pouring liquid antimicrobial products from conventional or reduced-splash containers for mixing or application purposes. The AEATF had revised the liquid pour protocol and consensus documents to address comments from EPA and the HSRB. The revised documents were submitted to Independent Investigational Review Board, Inc. (IIRB) and have been approved. Study recruitment is expected to begin during the week of February 6, 2012, and in-field monitoring is targeted to begin the week of February 12, 2012, and be completed by the end of February. The goal is to submit the report to EPA so that it can be reviewed in advance of the October 2012 meeting.

The Agricultural Handler Exposure Task Force (AHETF) has modified the protocol and supporting documents in response to Agency and HSRB review for the closed system liquid loading scenario that evaluates the dermal and inhalation exposure to workers who load liquid pesticides with closed-system equipment. The AHETF plans to submit the revised materials to IIRB in February 2012. Work has begun on compiling names for the Grower Universe List so that recruitment and monitoring can begin in southeastern states immediately after final approval. This protocol is dependent on seasonal timing of application using these closed systems, which occurs in the spring and summer. The AHETF anticipates finishing data collection in 2013 and submitting a completed report for review in 2014.

The completed No Mas-003 mosquito repellent study performed by Carroll-Loye Biological Research, Inc., was reviewed favorably by EPA and the HSRB. EPA is prepared to accept the registration application after it is submitted. The study is regarded as adequate to satisfy efficacy data requirements and evaluate label claims.

The Moiemen et al. study received favorable reviews from the Agency and the HSRB. This study was conducted with burn patients treated with dressings that included nanosilver. The purpose of the study was to evaluate the extent of dermal absorption of nanosilver. The HSRB concluded that the study can be used to support the Agency's conclusion that the dermal absorption of silver from nanosilver is less than 0.1 percent. EPA used the 0.1 percent dermal absorption factor in the risk assessment that supported the registration of HeiQ AGS-20, a textile preservative containing nanosilver. The conditional registration, issued in December 2011, is notable because it provides the first example of a quantitative risk assessment of a nanomaterial, and is the first pesticide product containing nanomaterials that EPA has registered knowingly. Mr. Jordan noted that HSRB efforts were very helpful with regard to this study.

Mr. Jordan discussed the status of the regulation promulgated by EPA in 2006 that has been the subject of litigation. EPA proposed a settlement of litigation to amend the regulation with minor modifications. The proposal was published for public comment in January 2011. Of the 10 public comments received, only two or three were relevant to the merits of the proposal. The Office of Management and Budget is in the process of completing an interagency review to provide an opportunity for other federal agencies (e.g., the Department of Health and Human Services and the Veterans Administration) to offer comments and express concerns. This proposal is expected to be finalized in the near future. If the modifications are finalized as proposed, these changes will not alter the work at EPA or the HSRB standards applied to studies.

Session 1: A new scenario design and associated protocol from the AHETF describing proposed research to measure dermal and inhalation exposure to workers, who mix, load and apply liquid pesticides with powered handgun equipment

Background

Ms. Kelly Sherman (OPP, EPA) noted that the Board would be discussing a new scenario design and associated protocol from the AHETF describing proposed research to measure dermal and inhalation exposure to professional agricultural workers who mix, load and apply liquid and solid pesticides with powered handgun equipment in managed horticultural facilities. The study will measure exposure to fungicides and insecticides used to treat foliage in open, enclosed or partially enclosed greenhouse and nursery settings. Existing exposure data do not meet the AHETF's requirements for inclusion in the Agricultural Handlers Exposure Database (AHED). The scenario consists of new data points, which are expected to be highly variable due to the diversity of application sites. The study will employ a 10 x 3 design consisting of three monitoring units (MUs) at each of 10 sites. Ms. Sherman noted that the protocol proposal, design objectives, rationale and procedures related to ethical conduct are very similar to previous studies reviewed by the HSRB.

EPA Science Assessment

Mr. Jeff Evans (OPP, EPA) noted that this is the first scenario to measure the exposure of workers, who mix, load and apply pesticides, which is common in small-scale operations. Workers will mix and load liquid and solid formulations and then apply the pesticides using powered handgun or hand wand equipment that is connected to tanks by hoses. The varied scenario will include treatments in greenhouses and open and partially enclosed nursery settings.

The baseline attire includes long-sleeved shirts, long pants, shoes and socks. Personal protective equipment (PPE) consisting of chemical resistant gloves will be worn by all workers. Additional PPE may include chemical resistant headgear in the event of overhead sprays; the AHETF will be informed ahead of time of overhead spraying, and patches will be used to estimate exposure to the subject's head. A chemical resistant apron may be worn for mixing and loading of some products, but this is expected to have minimal impact on exposure. The majority of the exposure is likely to come from mixing, spraying and incidental brushing against treated foliage. Protective eyewear may be worn, which also is expected to have minimal impact on exposure; a standard operating procedure (SOP) will be used to extrapolate exposure data.

Agricultural workers will be managing a hose connected to a sprayer to treat plants organized in a uniform manner in benches and hanging pots. Plants with similar sizes and growing characteristics are often grouped together. The capacity of the portable tanks will range from 25 to 150 gallons, and some will be carried on small carts or powered vehicles. Some hoses are managed by reels to connect the tank to the handgun or hand wand. The use of handguns results in pesticide application closer to the hand than the use of a hand wand, which has a longer barrel. Greenhouses will require an upward or downward spray pattern or an outward spray pattern if the plants are grown on benches. Nurseries will vary in the degree of openness, providing diversity of growing conditions. Partially open sites that contain structures to provide shade will be included in the scenario. The AHETF identified clusters of exposure sites across the United States, ranging from lower New England to Washington. Groups of counties delimiting a cluster location may include more than one state. This provides a wide range of climactic differences that may affect exposure.

Similarity restrictions for each cluster include provisions that MUs cannot be identical. Diversity exists in the facility type (e.g., nursery or greenhouse); mixing procedure (e.g., directly into the tank or premix and then transfer); hose attachment (e.g., hand wand or handgun); formulation type (e.g., liquid or solid); predominant spray type (e.g., downwards, outwards, or upwards); and whether equipment cleanup is performed. MUs within a cluster cannot be the same worker, have the same employer, or be based on the same degree of structural openness. Preferably, MUs will not use the same formulation type or be within the same amount of active ingredient handled (AaiH) stratum (e.g., 0.5 to 1.6 pounds, more than 1.6 up to 4.8 pounds, and more than 4.8 up to 15 pounds). Pesticides will be selected from a predetermined surrogate product list that includes a variety of insecticides and fungicides. All pesticides can be used safely under the conditions of the proposed studies. Analytical methods for dosimetry have been evaluated (methods for permethrin and azoxystrobin are in development). Dosimetry will consist of six sections of whole body dosimeters, patches, socks, hand rinses, face and neck wipes, and Occupational Safety and Health Administration (OSHA) Versatile Sampler (OVS) tubes.

Mr. Evans emphasized that this is a highly varied scenario in regards to structures, spray patterns and the type of plants treated. Mixing, loading and application of pesticides by the same person is the industry standard. The study includes provisions for liquid and dry formulations, and subjects will handle small amounts of active ingredient (AI). Application of the pesticide is expected to be the predominant contribution to exposure. However, EPA requests that the Board address the recommendation to include a wettable powder formulation in at least one MU per cluster due to the potential for higher inhalation exposure that is not mitigated by aprons or other PPE.

In conclusion, EPA found the study to be scientifically acceptable. The scenario is well defined, and the study is likely to produce reliable mixer and loader applicator data to assess the potential exposure of handlers using powered handgun or hand wand equipment.

<u>Board Questions of Clarification—Science</u>

Dr. Chambers asked why the wettable powders might lead to higher exposures. Mr. Evans responded that previous studies from the Pesticide Handler Exposure Database (PHED) have found inhalation levels to be much higher for powder formulations because they

are dustier than liquids. An analogy would be to compare the dust that arises from pouring flour into a bowl versus pouring liquid into a bowl. This AHETF study provides an opportunity to determine whether the physical process of wetting a powder formulation affects exposure. Mr. Evans clarified for Dr. William Popendorf that the previous PHED studies indicated an increase in exposure of two orders of magnitude for mixing, loading and applying a powder formulation. Dr. Linda Young asked whether the data on wettable powders would be used separately when making recommendations. Mr. Evans responded that if the data are different between wettable powder and liquid formulations, they may add the powder component to the scenario to assess exposures.

Dr. Dallas Johnson cautioned that the inclusion of liquid and solid formulations might result in two studies, one with 10 clusters of one MU and the other with 10 clusters of two MUs. He questioned whether the risk assessment would be adequate with those data. Dr. Philpott remarked that he was unsure if the Agency has considered that issue and thus could respond as to whether or not the risk assessment would be adequate. Rather, Dr. Philpott believed, this may be one of the Board's recommendations to the Agency . Mr. Evans welcomed remarks from the Board and noted that the risk assessment would rely on all 30 data points for a conservative estimate. The topic was tabled for later discussion.

Dr. Rebecca Parkin requested clarification as to whether all participants will use headgear, including a face shield, and if there would be variation in the type of headgear. Mr. Evans replied that headgear would be varied. There are many types of chemical resistant purifying respirators. Some headgear contains chemical resistant fabric and some cover the head with a flap on the back. Air purifying respirators are common and may have a cooling effect. Mr. Evans was unsure whether respirators would be used because the pesticide products may not require use of a respirator. Dr. Parkin asked Mr. Evans if he was satisfied that there was sufficient documentation of the variety of headgear in the study, and Mr. Evans affirmed that documenting headgear would be important. Dr. Popendorf questioned if adjustments would be made for subjects wearing half-mask respirators. Dr. Evans responded affirmatively that there is a provision within the protocol to adjust for that situation.

Dr. Popendorf questioned whether the European Crop Protection Association (ECPA) data regarding pesticide application exposure levels could be combined with the separate mixer/loader data to meet the data requirements of EPA. Mr. Evans thought that it would be useful to compare the data within the ECPA database.

Dr. Sidney Green requested clarification regarding the asterisk that appeared slide 19 of EPA's Science Assessment presentation detailing the outward, downward and upward directions of spray. Mr. Evans stated that the asterisk likely indicated that an upward spray pattern would require the use of chemical resistant headgear.

Dr. Green mentioned that the proposal objectives applied to dermal toxicity and he questioned the rationale for why inhalation toxicity was treated differently from dermal toxicity. Mr. Evans clarified that the study was not measuring toxicity, just exposure through the dermal or inhalation route. The AHETF will perform proportionality and relative fold accuracy tests for inhalation to evaluate whether those data can be used, but Mr. Evans noted that dermal contact is the primary route of exposure for most studies of this nature. The relative fold accuracy requirements may be larger for inhalation exposure.

Dr. Jewell Halanych noticed that the protocol included the option of pesticide application by walking or riding in a vehicle. She questioned whether differential exposure may occur in the two situations. Mr. Evans explained that EPA was satisfied that the protocol captures all variability limited to handgun equipment in regards to spray direction and so forth, but although it would be interesting to assess, evaluating the option of walking or riding is beyond the limits of the scenario.

Dr. Philpott noted that one picture from Mr. Evans' presentation depicted two workers applying product simultaneously and wondered whether the presence of multiple applicators may affect the data in this monitoring scenario. Mr. Evans replied that worker protection standards in the United States require that workers apply product alone, with distance requirements existing for others within the spray vicinity. The picture referred to by Dr. Philpott was taken in Mexico where requirements are different.

EPA Ethics Assessment

Ms. Sherman stated that additional data are needed to improve EPA's ability to assess safety and risk associated with these application scenarios, and this scenario will consist of all new data to better estimate dermal and inhalation exposure for a wide range of pesticides. The data will be used to populate the AHED database, in which similar data do not exist. There is a broad applicability due to the diversity of test sites and application scenarios and the study will provide value to society.

Subjects will be selected by identifying eligible commercial growers and contacting them by telephone to discuss potential interest in the study. The growers will be required to sign a non-coercion statement. Subjects will be recruited among employees who have experience within the past year with mixing, loading and applying pesticides using powered handgun equipment. The subjects also must meet the other eligibility criteria specified in the protocol. Permission will be sought to approach employees of eligible growers, at which point prospective subjects will be contacted directly and flyers will be posted. A recruitment meeting with interested employees will be held on site in the absence of supervisors to explain the basic principles, procedures, risks and benefits of the research. If prospective subjects choose to continue, a private consent interview will be conducted between the employee and the investigators in the employee's preferred language of English or Spanish. Similar to procedures followed by the AHETF in other protocols, the consent form containing all elements required by 40 Code of Federal Regulations (CFR) §26.1116 will be explained to each subject.

Ms. Sherman noted that the organization and presentation of risk information contained in the consent forms is thorough and acceptable. Five categories of risk are outlined in the protocol, and measures to protect against these risks are sufficient. Heat-related illness is a concern because the extra layer of clothing worn by the subjects might raise body temperature. An SOP for monitoring the heat index will be followed, and the monitoring will be stopped if the temperature rises above a 105 degrees Fahrenheit (°F) heat index. A medical professional will be on site to provide care. The second and third risk categories detail exposure to pesticides and surfactants. Protections against those risks consist of excluding subjects with sensitivity to these substances, selecting handlers in good health, and requiring that subjects be experienced with the equipment. The fourth risk category involves scripting of field activities. The workers will be performing their normal task of employment, but they might be changing their behavior slightly by applying more or less product than usual to establish the variability needed for the

study. EPA decided that this was a small additional risk. The fifth risk described psychological hazards, including the possibility of breach of privacy or unwanted disclosure of pregnancy results. The protocol details methods to mitigate these risks and protect subject privacy by handling test results discretely and ensuring that identifiable characteristics of the subject are obscured in photographs. Ms. Sherman reiterated that the risks of this study are adequately explained and appropriately minimized.

Although there are no direct benefits to the subjects of the study, sponsors will benefit from improved risk assessments that accurately reflect actual exposure. The likely societal benefit includes higher quality exposure and risk assessments for pesticides that are mixed, loaded and applied using handheld equipment in greenhouses and nurseries. Regarding risk-benefit balance, the risk to subjects is low and can be considered reasonable given the potential societal benefits. Subjects will be paid a reasonable amount of $20 to participate in the consent interview and $80 to participate in the study, and will be informed that they can withdraw at any time without loss of payment providing that they suit up with the dosimeter. The protocol indicates that medical care for research-related injuries will be provided at no cost to the subjects.

The protocol was reviewed and approved by IIRB, which is an accredited ethics committee independent of the study sponsors and investigators. IIRB's "Human Research Protection Program Plan" and the current membership roster have been provided to the HSRB along with background materials. This proposal is for third-party research involving intentional exposure of human subjects to a pesticide, with the intention of submitting the resulting data to EPA under the pesticide laws; therefore, the primary ethical standards applicable to the conduct of this research are 40 CFR part 26, subparts K and L, and the Federal Insecticide, Fungicide and Rodenticide Act (FIRFA) 12(a)(2)(P).

EPA requested that future protocols be revised in three ways. First, the protocol should clarify the discussion of "psychological risks." Breach of confidentiality should be added to the discussion of psychological risk, and the protocol needs to clarify what is meant by risk of pregnancy testing. The wording should be crafted differently to indicate that psychological risk in regards to pregnancy testing refers to unwanted disclosure of pregnancy test results rather than risk of embarrassment. Second, the protocol should specify where the recruitment discussions between researchers and potential subjects will occur; ideally, the site will be separate from the work site so that influence from employers is minimized. Finally, criteria should be developed for medical professionals to determine if a subject is too sick to refuse medical treatment, and the criteria should be documented in an SOP. Ms. Sherman noted that none of these provisions will prevent approval of the current protocol, but should be included in future protocols.

In conclusion, Ms. Sherman indicated that EPA has adequate information to conclude that the protocol meets substantial compliance with subparts K and L for 40 CFR part 26.

Board Questions of Clarification—Ethics

Dr. Virginia Ashby Sharpe noted that the risk mitigation detailed in the proposal addressed the problems that would have been associated with the psychological risk of unwanted exposure by the fact that identifying features would be obscured in photographs and pregnancy test results would be handled discretely. Ms. Sherman agreed that the protections are in place; however, the details of the risks are not described adequately and the description in the protocol needs to be modified. Dr. Philpott noted that an additional psychological risk would be embarrassment associated with disrobing in front of an observer to collect the dosimeter. He agreed that there was confusion in the protocol section describing psychological risk and this topic would be revisited in the Board discussion.

Dr. Sharpe requested confirmation that "open pour" will be the method used for mixing and loading, and Mr. Evans verified that was correct.

Questions for Researchers

Dr. Philpott invited the study sponsors Drs. Victor Cañez and Richard Collier to the table to answer Board questions regarding study design and ethics. Drs. Cañez and Collier introduced themselves, noting that they were speaking on behalf of the AHETF.

Dr. Chambers asked how easy it was to recruit subjects for this scenario. Dr. Cañez replied that it was no easier than for other studies, but they had an advantage of a finite and easily obtained list of growers. He noted that if the growers meet the criteria for the surrogates and are willing to participate, difficulties in recruiting should be minimial.

Dr. Popendorf asked if Drs. Cañez and Collier were knowlegdeable about the ECPA database, and if they have identified restrictions with use of the European data. Dr. Cañez explained that they evaluated the data available in the ECPA database. After surveying greenhouse and nursery practices, they realized that the person who mixes and loads also does the applying. They determined that separating the mixing/loading exposure monitoring from the application exposure monitoring may create artificial situations. Additionally, interference with workers will be reduced by monitoring one person performing all tasks rather than monitoring two people (i.e., one who is mixing/loading and the other who is applying pesticide). Dr. Popendorf clarified that he was suggesting that the AHETF and the Agency use the ECPA applicator data in conjunction with the existing AHETF mixer/loader data to measure exposure for these scenarios, thus precluding the need to collect new data. He questioned whether there were any factors that would preclude the use of combining databases for this purpose. Dr. Cañez replied that there were variations in the PPE used in the other studies, causing confounding issues in addition to the artificial separation of tasks. This point was tabled for Board discussion.

Dr. Philpott questioned the reasonability of applying a 105°F heat index cutoff if the workers are operating within greenhouses where high temperatures are likely. Dr. Cañez agreed that high humidity levels may restrict the application time to morning, evening or night.

Public Comments

Dr. Cañez noted that he enjoys the HSRB meetings and has learned a lot through his interactions with the Board. He will miss the four Board members who are departing. Dr. Collier

repeated Dr. Cañez's sentiments and expressed gratitude to all of the Board members. He noted that the protocols are substantial and complex, and he appreciates the Board's effort to give good advice to the sponsors and the Agency.

Dr. Philpott asked if anyone else present would like to comment on the AHETF study. No additional public comments were made. Dr. Philpott noted that one written public comment was received, but the substance of the content was not directly related to the two protocols under review by the HSRB. The comment is available on the docket.

Charge Questions

Ms. Sherman read the charge questions into the record:

If the proposed research is revised as suggested in EPA's review and the research is performed as described:

- Is the research likely to generate scientifically reliable data, useful for assessing the exposure of workers mixing, loading and applying pesticides in managed horticultural facilities using powered handgun equipment?

- Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

Board Science Review

Dr. Philpott asked Dr. Chambers, as Lead Science Discussant, to address the first charge question. Dr. Chambers began the discussion by indicating that she has appreciated the privilege to serve on the Board, and values the friendship of the Agency, sponsors and Board members. She will miss them when her term is complete.

Dr. Chambers asserted that the answer to the first charge question was affirmative. The protocol was well planned and well designed, reflecting iterations in protocols over the past few years. Noting that the investigators found no suitable existing information that could constitute the monitoring units for this scenario, the entire scenario has to be conducted. The design provides for three MUs across 10 different regions for a total of 30 MUs. She rationalized that this was because few nurseries and greenhouses would be suitable for the study. Due to the diverse types of scenarios, she expects that exposure numbers will be widely varied. The design is similar to other protocols in the objective to demonstrate proportionality between exposure and AaiH. Dr. Chambers noted that incidental exposures, not unlike those seen with roadside spraying as in an AHEFT protocol previously reviewed by the Board, may be important to consider in the analysis. Unintended contact with foliage needs to be observed, documented and evaluated to determine if it can explain some of the diversity in the exposure values. Another consideration is the added exposure resulting from equipment cleanup. She noted that the AaiH limit of 15 pounds seems smaller than what would be required for many outdoor situations, and merging high-level mixing/loading exposure data in the ECPA with low-level nursery application exposure data for risk assessment may not be viable due to the different scales of magnitude. In conclusion, Dr. Chambers assessed that the protocol was well designed, well written and will yield valuable information.

Dr. Philpott asked if Dr. Green, as Associate Discussant on this protocol, if he had any additional comments or recommendations for the Agency. Dr. Green agreed with the scope of Dr. Chambers' discussion.

In discussing statistics, Dr. Young returned to the question of whether wettable powders differ substantially from liquids. She noted that this was an important question regarding the study design. Dr. Young presented a few slides to illustrate her point regarding the separation of data. She demonstrated that the wettable powder has a different intercept than the liquid formulation with standard deviation on a log-based scale. If data like these are generated in the current study, it would be useful to differentiate the two formulations. However, she noted that changing the standard deviation of the data by one unit of log exposure was enough to obscure any differences between wettable powders and liquids. Additional observation of wettable powder MUs may be needed to decrease the standard deviation enough to observe a measurable difference given the diversity of exposure scenarios. EPA should consider the importance of measuring differences in formulation type and whether the differences may be obscured due to the scenario's diversity.

Dr. Young added that a common question raised by the HSRB is whether there is enough power to estimate exposure with a certain level of precision. However, this study is not evaluating power. She suggested broadening the sample size to include adequate precision or power, whichever is applicable.

Dr. Johnson applauded the study for its relatively broad decision to monitor 10 clusters of three MUs apiece. He echoed Dr. Young's concern about whether there would be a big difference between the powder and liquid formulations. He noted that the Agency is recommending that every cluster include one powdered formulation. Dr. Johnson questioned whether it would be better to have 15 solid and 15 liquid MUs. If it is likely that powder will cause higher levels of exposure than liquid, perhaps all of the MUs should use powder formulations to generate a conservative estimate. Another option would be to have two separate studies, one involving powder and one involving liquid formulations. It may not be possible to make that decision now; perhaps a second study will be initiated based on the results of the first. Mr. Evans replied that they have evaluated all of those considerations and they are confident that many aerosolized particles will be captured by the OVS tubes. He asserted that product application is the largest proportion of exposure.

Dr. Philpott noted this was a fundamental question, and summarized the recommendations of Drs. Johnson and Young. He noted that the Board is raising concerns about the assumption that greater inhalation exposure will result from mixing and loading powder versus liquid formulations, and the impact of this difference is as yet unknown. A simple change in standard deviation may mask any effects of wettable powders. Dr. Johnson responded that it appears that EPA has considered these implications and realizes that additional data might be needed. Dr. Philpott noted that the Board's report will provide careful consideration to this issue and the potential impact on the Agency's analysis of the data.

Dr. Popendorf suggested that the solid or liquid formulation variable in the study is just one example of how the diversity of variables in the scenario might complicate data analysis. He considers the biggest variables to be the direction of application and whether the subject cleans the equipment afterward. The proximity of the hand to the spray and the degree of enclosure are other important variables. Dr. Popendorf considers the liquid or solid powder to be less

important, albeit relevant. He questioned whether the study design is intended to maximize variability or if the intent was to separate variables. Dr. Young requested that EPA clarify if the intent was indeed to separate the variables. Mr. Evans responded that the data will be used for decision making and, to that effect, wettable powder may be important and regulatable. There is less control over regulation of variety in handguns. Mr. Evans agreed that with the diversity of scenarios, it might not be possible to see separate effects. He noted that any comments from the Board about how to approach the data analysis are appreciated. Dr. Young responded that EPA should analyze the data separately and then together. Combining the data will increase variability to the extent that it may be obscured in the analysis.

Dr. Popendorf revisited the issue related to the use of data within the ECPA database. He agreed with Dr. Chambers that the use of mixer/loader data will not have a large impact on the data generated, and he recommended that EPA consider combining the European applicator data and AHETF mixer/loader data, thus precluding the need for this study.

Dr. Popendorf addressed the use of protective hats in the study. He noted that the topic was reviewed in October 2010 when the Board discussed limitations to estimating the exposure of people with and without hats. If hats are worn in monitoring scenarios, exposure to people not wearing hats will be underestimated. Dr. Popendorf recommended that this issue be addressed in the protocol under discussion. He noted that subjects could use a chemical resistant hat without a brim, or the exposure of the area of the head beneath the shadow of the brim could be monitored with a patch to better quantify exposure without a hat.

Dr. Chambers asserted that because of the diversity and possibility of incidental exposures, proportionality may not be observed. Nevertheless, she reiterated that the study is well designed and will generate high quality and useful data for EPA to use in risk assessments.

Dr. Lebowitz initiated a discussion about what should be considered “incidental” exposures. Brushing against equipment while mixing, loading and touching treated plants may be critical in determining excesses of exposure and defining differences between individuals. He questioned whether recording incidental events would be sufficient to detect the contribution of each source of variability. Mr. Evans reiterated that the biggest driver of exposure is the AaiH. He affirmed that good observations are critical for informing conclusions in this type of study.

Dr. Philpott summarized the Board’s opinion, noting that the answer to the charge question is that the study will generate reliable and useful data, but there are caveats for the Agency and sponsors to consider. The first caveat considers potential sources of diversity in exposure. The Board recognizes that the Agency is operating on the assumption that AaiH is the predominant driver of exposure, but other variables might obscure the results and prevent the observation of proportionality. The Board recommended that the Agency and sponsors observe and record all cases of incidental exposures as uniformly as possible. Dr. Philpott continued, noting that the statisticians are concerned about the use of powder and liquid formulations. He repeated Dr. Young’s request that the data be analyzed separately first and then together. The Board suggested standardizing the use of hats without a brim if in compliance with worker’s regulations, or adding another patch below the brim and shadow of the brim. The data within the ECPA database has been discussed in regards to whether justification exists for the study given the data available. The Board’s recommendation is for the study sponsor and EPA to revisit those data to ensure that they do not answer the questions asked by the study before proceeding. The

broader issue will be how to incorporate results from this study with the ECPA evidence in regards to the overall weight of evidence.

Dr. Popendorf added that the Board should clarify the terminology of incidental exposure. This could mean exposure to a chemical unrelated to the amount used, including exposure to residues on equipment surfaces. The amount of exposure from brushing against recently treated foliage could be related to the amount of product applied. Dr. Chambers clarified that brushing against a treated plant would be considered an incidental exposure because that behavior is meant to be avoided. Dr. Lebowitz emphasized that the incidental exposures might be critical to the outcome of the study and may preclude the observation of proportionality. Dr. Philpott asserted that the Board discussants and Chair will work together to craft a mutually agreeable definition for incidental versus other types of exposures.

Dr. Parkin questioned if Dr. Popendorf was suggesting that the Board should require additional written justification from EPA regarding the use of ECPA data. Dr. Philpott replied that he did not believe that the Board was not going to require further justification from EPA. Dr. Popendorf had suggested a formal review of the data available and to document the impact on the study, but the Board will not require additional written rationale. Rather, the Board will defer to the Agency and sponsors in their expert opinions that the study is justified. Dr. Sharpe noted that the question of whether the study was necessary given the ECPA data was a difficult question. She is confident that the Agency and sponsors will address the concern. Dr. Philpott concluded that the consensus position of the Board that no further justification or approval by the HSRB was necessary to move forward with the study.

Board Ethics Review

Dr. Philpott asked Dr. Sharpe, as Lead Ethics Discussant, to address the charge question that asked whether the research was likely to meet the applicable requirements of 40 CFR part 26, subparts K and L. Dr. Sharpe stated that it is likely that the research will meet ethical requirements. She opened a discussion about suggested modifications to the informed consent form, noting that the consent form does not contain information about adverse reactions. Dr. Sharpe suggested that the Board consider whether language should be included about the name and contact information of the study director if the subject experiences adverse effects within 24 hours. Dr. Sharpe and Ms. Sherman discussed whether the information about adverse reactions was present in the consent form. Dr. Philpott concurred that the language regarding adverse reactions should be on the consent form and, if it is not there, it should be added. The Board agreed with this recommendation.

Dr. Sharpe noted that the language in the protocol relevant to the timing of the pregnancy test prior to the start of the study is adequate, but language in the consent form is unclear. The consent form states that pregnancy tests should be conducted within 24 hours of the study, but this could be interpreted in such a way to allow testing to occur following completion of the study. and Dr. Sharpe recommended that it should be modified to say 24 hours prior to starting the study. She also noted that the language on the consent form should say “In order to take part in the study…” rather than “If you do take part in the study…” With the exception of these minor modifications, Dr. Sharpe was satisfied with the consent form.

Dr. Sharpe agreed with EPA recommendations that the protocol should define the off-work site at which consent takes place and the SOP should include the criteria for determining if a

subject is too sick to refuse medical treatment. She disagreed that the Agency's concern that the language in the protocol describing psychological risk is inadequate. Dr. Sharpe noted that sufficient risk mitigation procedures were detailed in the protocol, and describing them further might cause undue anxiety to participants. Many steps have been taken to ensure confidentiality, so emphasizing the parameters in place for dealing with breach of confidentiality may be superfluous. Dr. Philpott concurred that adding language to the consent form clarifying risks could overly emphasize the risks of study participation and thus make subjects anxious. Ms. Sherman clarified that the suggestion was to improve the language in the protocol, not the consent form. The comment had resulted from a discussion with Dr. Lux regarding true psychological risk. Ms. Sherman agreed that too much detail in the consent form is unnecessary. Dr. Philpott asked if the Board agreed that the information in the consent form regarding risk was adequate. Dr. Sharpe and the other Board members concurred. Dr. Halanych also voiced her approval of the information in the consent form being sufficient in regards to the description of risk.

Dr. Philpott reiterated that the Board's response to the ethic charge question is affirmative; if the study is amended as discussed and conducted as designed, it will likely be in agreement with 40 CFR part 26, subparts K and L. He noted general agreement that the sponsors should clarify where informed consent will take place and develop clear criteria for assessing the capacity for a subject to refuse medical treatment by a medical officer. The consent form is sufficient, with minor suggestions, to ensure informed consent by participants. The protocol, but not the consent form, will be clarified in the discussion of risk.

Session 2: A completed scenario monograph and study report from the AEATF II in which the dermal and inhalation exposure of professional janitorial workers was monitored as they applied a liquid antimicrobial pesticide product for indoor surface disinfecting using a pressurized aerosol can

Background and EPA Science Assessment

Mr. Timothy Leighton (OPP, EPA) noted that the Board will review a completed study from the AEATF that monitored exposure of workers spraying various indoor surfaces with aerosol cans. The HSRB had reviewed the initial proposal for this study, monitoring exposure of workers spraying aerosolized disinfectants, in October 2009. He introduced Dr. Jonathan Cohen, who served as the statistician for the review and who was available via telephone. Dr. Leighton acknowledged the Joint Regulatory Committee, with participants from Health Canada, California Department of Pesticide Regulation (CDPR) and EPA, for their work on the aerosol study.

Mr. Leighton noted that this completed aerosol scenario was one of 17 AEATF exposure scenarios. He noted that the AEATF has acted on recommendations proffered by the HSRB for the liquid pour study reviewed in October 2011 and that study will begin in 2 weeks. The AEATF is working hard to get studies moving forward. The current scenario monitored spraying indoor surfaces (e.g., showers, sinks, countertops and so forth) with an aerosol spray can but excluded the wiping of sprayed surfaces, which was monitored as a different scenario.
Mr. Leighton asserted that the lack of wiping was an important consideration because some products sprayed with an aerosol can do not need to be wiped. Workers might be accustomed to wiping after product application; however, special attention was paid to the recorded observations, which noted that no workers wiped surfaces after they were sprayed.

The aerosol study was conducted at three randomly selected hotels in Fresno County, California, including a Marriott hotel, a Piccadilly Inn and a Hilton hotel. The study was stratified by six independent monitoring events (MEs) at each of three sites. To ensure diversity of individual exposures, at each site one enrolled subject was assigned to one of six MEs defined by the number of cans sprayed, ranging from one can to four cans. Some cans were emptied halfway and weighed prior to the start of the ME to account for slight differences in the amount of product applied. The dermal and inhalation exposure to Clorox disinfecting spray (n-alkyl dimethyl benzyl ammonium chloride [ADBAC]) was monitored using six inner/outer whole body dosimeters. Other clothing requirements included long pants, long-sleeved shirt and no gloves. Subjects wore two breathing zone air samplers, OVS tubes and RespiCon Particle Samplers (RPSs). Notably, the OVS tubes process 2 liters per minute while RPSs process 3 liters per minute.

The aerosol protocol's study objective was to have sample estimates of the arithmetic mean and 95th percentile of normalized exposure accurate to within three-fold 95 percent of the time. The AEATF discussed the SOP with the HSRB early in the process and responded to EPA comments. EPA recommended that the AEATF indicate the course of action if the benchmark accuracy goals (i.e., a K-factor of 3) are not achieved. The AEATF responded that they will work with EPA to determine the course of action, including collecting additional data, if the accuracy goals were not met.

In its original review of the protocol, the HSRB had noted that many variables might affect exposure and the Board wanted to know if results could be generalized for consumers. Mr. Leighton noted that, ideally, the two populations would be monitored in parallel. However, the EPA accepts the data for consumers because the spray behavior for a consumer is not expected to deviate from that of a janitorial worker due to aerosol spray cans being easy to use. The AEATF assessed the observation data to determine that no behaviors were performed by workers that would be inconsistent with the behavior of a consumer. Workers experienced incidental exposures from leaning on surfaces and brushing against shower curtains similar to what consumers would experience. Additionally, labels on the aerosol cans do not distinguish workers from consumers, so monitoring the exposure of janitorial service workers who apply multiple cans at a time will ensure that product labels are appropriate for both cohorts and will provide a more conservative estimate of exposure for consumers.

The HSRB also had noted in its prior review that they could not judge the sample size adequacy without a statistical analysis plan. The AEATF responded that they will use the base set of data to determine the sample size, and acknowledge that additional data collection might be required. The HSRB also requested clarification of the details regarding spray application, which was provided by the AEATF in the revised protocol and in two letters that are appended to the EPA Science Review. Clarifications resulting from HSRB comments included the designation of hotels as study sites, the limit of two MEs per day, and the specification of the number of cans sprayed at a time.

Regarding quality assurance improvements, the AEATF increased the minimum fortification levels from two-fold to four-fold limitation of quantitation (LOQ), ensured that surfaces were dry prior to application, and recorded careful observations. Mr. Leighton noted that additional improvements resulting from HSRB comments could be read in the study report.

The completed aerosol study reported 18 deviations in protocol, methods and SOP, none of which affected scientific validity. The order in which the number of cans sprayed was reversed in one of the clusters to ensure there were enough MEs. Hand wash and wipe removal efficiency studies were modified to address the EPA Science Review. Hand washes were performed with a 30-minute drying time. Solubility of the quaternary ammonia products was a concern, but the AEATF responded that they are all soluble up to 2 percent in an isopropyl alcohol (IPA)/water solution. Products of less than 2 percent were used in the scenario. The two wipe efficiency studies, **didecyl dimethyl ammonium chloride** (DDAC) and alkyl dimethyl benzyl ammonium salt (ADBAS), show conflicting results. The difference may have resulted from the fact that the ADBAS study measured the wipe removal efficiency directly from the skin, as opposed to the DDAC wipe portion of the study that measured wipe efficiency after fortified hands were dried for 30 minutes and then washed, resulting in a 10 percent residue of the initial fortification remaining on the hands. When that amount was wiped off, a 60 percent recovery was calculated for the wipe. In the ADBAS study, hands were fortified, dried for 30 minutes, and wiped directly to remove 90 percent of the fortification. Finally, the drying time in removal efficiency studies came under consideration, but according to literature, a range of drying time from 30 minutes to 2 hours should not significantly affect removal efficiencies because DDAC dermal penetration is less than 1 percent.

Study participants wore whole body dosimeters under and on top of long pants, long-sleeved shirts and no gloves. The dermal unit exposures (UEs) can be estimated for three clothing configurations due to the placement of the whole body dosimeters: long pants with a long-sleeved shirt, long pants with a short-sleeved shirt, and short pants with a short-sleeved shirt. The mean AaiH was 0.0031 pounds, with a range from 0.0013 to 0.0053 pounds. The mean ME duration was 70 minutes, with a range from 25 to 128 minutes. The mean surface area sprayed was 1,282 square feet, with a range from 417 to 2,419 square feet. Rather than using nominal concentrations, the investigators measured the percent AI and the weight in the cans to calculate AaiH of ADBAC accurately.

Mr. Leighton noted that all laboratory and field controls were less than the LOQ. The samples had satisfactory LOQs, indicating that non-detects were not a problem. Laboratory recovery rates ranged from 90 to 100 percent with a few outliers. Field recoveries were collected and processed in parallel with samples to correct dosimetry samples. The mean recovery for all samples was 90 percent, similar to previous studies. Two outliers were discarded from the analysis.

Regarding statistical evidence, three methods were used to estimate UEs: empirical estimates, simple random sample and mixed model methods. Empirical estimates were used to look at individual data points, which is useful to ensure data transparency. Mr. Leighton noted that the public may be looking at the data in addition to statisticians. If the mixed model is drastically different from the empirical estimate, the public will want to know why. Similar values between models facilitate transparency. The mixed model was selected to best represent the UE results.

Of the 108 sections analyzed for dermal exposure, 87 percent had detectable values, indicating that the study was designed adequately to detect residues. The LOQ was adequate for the study. One of the monitoring clusters had exposure levels much higher than the rest, but the data were included in the analysis because none of the behavior observations were considered negligent. The potential impact of this one cluster is 10 percent.

Inhalation exposure was measured using values for spray time instead of sampling time to correct for variations in spray speed between subjects. Because the monitor ran the entire time, it was more appropriate to use sampling time for the calculations. The calculated arithmetic mean for inhalation using sampling time was 60.3 milligram per cubic meter per pound ($mg/m^3/lb$) AI.

Mr. Leighton discussed whether the sample size was large enough based on the data. He noted that the benchmark objective of three-fold relative accuracy (K-factor is less than or equal to 3) was met for the mixed-model results using the study design of three clusters each with six MEs. Because the relative accuracy was less than three, there was no need for additional data collection.

The aerosol data are not inconsistent with the assumption of proportionality. Proportionality between exposure and AaiH is used by EPA to extrapolate the data to other chemical exposure assessments. Results of the aerosol study support this assumption. The relationship between dermal exposure and AaiH shows evidence of proportionality with a slope of approximately one. The Board had suggested looking at inhalation as a dose, not in terms of air concentration. There is a suggested proportional relationship between inhalation dose (measured in mg) and AaiH, although the slope is 1.5 with a confidence interval (CI) from 1.05 to 1.84. There is no evidence for proportionality between air concentration (measured in mg/m^3) and AaiH, although the CI included zero. Time weighting those averages, however, generates a slope similar to that of the inhalation dose because time has been factored into the equation.

Data generalization from this study has limitations. For example, the aerosol study population is not a random sample due to the assumption that exposure is independent of location. Notably, statistical inference from these results to all people who spray with an aerosol can is not justifiable and was not a goal of the study. The study assumes that the location of Fresno, California, is not much different than any other city, and the sprayable surfaces within buildings are not going to be significantly different.

EPA plans to use the UE data from the aerosol study to estimate potential exposure to low- or moderate-volatility pesticides use in aerosol scenarios. The data will not be used to assess fumigants. Dermal UE values are available for various clothing configurations. Inhalation exposure is still being evaluated by EPA, but preliminary results suggest that a factor of 1.25 separates the OVS and RPS values. The two air samplers agree fairly well in the measurement of 100 micrometer (µm) particles. The AEATF is uncertain whether the data should be corrected by that factor and welcomes advice from the Board. EPA plans to use UEs normalized by pounds AI values in collaboration with chemical-specific hazard and dermal absorption values to estimate the internal dose and risk from these data.

In conclusion, EPA determined that the study results are sufficiently sound to support estimates of dermal and inhalation UEs. An adequate number of samples were collected, thus precluding the collection of additional aerosol MEs and certifying the use of the data now. Mr. Leighton acknowledged the data limitations.

Board Questions of Clarification—Science

Dr. Philpott noted that Dr. Menikoff had joined the Board, and then opened the floor for questions of clarification.

Dr. Young requested clarification regarding whether the proportionality between exposure and AaiH was on a log scale in Figure 9 within the EPA Science Review. Dr. Cohen responded affirmatively: the straight purple line is the log of exposure regressed using a mixed model against the log of AaiH normalized such that the slope of log exposure is one. The curved green line in the same graph indicates an arbitrary slope and intercept for log of exposure related to log of AaiH. Dr. Young asked if the curved green line indicated a quadratic fit on the log-log scale. Dr. Cohen responded that was not correct. Dr. Cohen explained the equations for the models representing the two different lines in the graph. The models are included in Appendix A of the EPA Science Review. The point of the purple line is that exposure and AaiH are assumed to be normally distributed. The green line does not assume a slope of one, but is based upon a model where the exposure is equal to some constant times AaiH is raised to the power of the slope of the line. The data are proportional in the log-log scale. Dr. Johnson clarified that the purple line does not depend on data other than the intercept, and Dr. Cohen said that was correct. He explained that after the mean of exposure and AaiH is calculated and the constant K is defined, then AaiH multiplied by K can be used to estimate exposure. Dr. Johnson clarified that the green line resulted from the actual data. He explained that he had trouble determining if the figure was labeled correctly because the line would be straight unless plotted on a log scale.

Dr. Young raised concern with the slope of the relationship between inhalation dose and AaiH not being equal to one with a wide CI. Mr. Leighton responded that was the cause of using the terminology of “suggested” rather than “evidence” of a proportional relationship.

Dr. Popendorf asked if the workers had to be experienced. Mr. Leighton responded that the subjects were recruited from janitorial maintenance services. Dr. Popendorf noted that there was a fair amount of diversity in the subjects.

Dr. Popendorf stated that the number of non-detected values was small, and because all of the non-detects in the inner dosimeter were 10-fold lower than the unusually high inner dosimeter values for subject AE19, the effect of the non-detected values was negligible. Mr. Leighton replied that application of three methods of statistical analysis did not make a difference in the overall evaluation. Only 13 percent of the inner dosimeters did not function; the results were driven by the higher exposure values.

Dr. Popendorf noticed that the average time taken to treat each room was significantly different at one of the sites. Two of the sites had an average of 8.5 minutes per room, but the last site had an average of 6 minutes per room. He questioned whether that was because one of the sites had a different layout than the other two. Mr. Leighton noted that the hotel with faster times was the Hilton hotel. He suggested that they revisit the question during the public comment period.

Dr. Johnson asked Mr. Leighton to elaborate on Figures 6 and 7 of the EPA Science Review. Mr. Leighton referred the query to Dr. Cohen, who explained that Figure 6 represented the log of dermal exposure plotted against the log of AaiH. The line in the figure indicates the fitted regression line in log-log scale. Notably, the fitted lines from the simple linear regression model and the mixed model are the same, indicating that there is no cluster effect. Dr. Johnson thanked him for

the clarification. Dr. Johnson asked about the models within Appendix A of the EPA Science Review. Dr. Cohen clarified that the results of the spray duration are not within statistical review because the inhalation dose was corrected by multiplying by sampling time rather than spray duration. Dr. Young questioned the genesis of the "half" value that is multiplied by variance within the models. Dr. Cohen answered that is done to calculate the arithmetic mean of the ratio of the exposure divided by the AaiH. If the variance of the log of exposure is V, then the expected value of the UE is given by E to the intercept times E to the half of the variance. This equation results from log-normal distribution models.

Dr. Lebowitz asked how the EPA analysis accounted for the sample outliers of laboratory recovery values. Mr. Leighton explained that the laboratory recovery outliers were included in the analysis, and were not used to correct field samples because the field recovery samples were used to cover both the laboratory and the field samples. Dr. Lebowitz confirmed that the two very high field recoveries were not included in the analysis, and Mr. Leighton concurred. Dr. Lebowitz asked how the samples are used to correct the data. Mr. Leighton explained that each sampling matrix, including the whole body dosimeters, the hand wash, the wipes, and the air, had their own set of fortifications for the field recoveries. Each one was used as an average to correct samples themselves. If the field recoveries came back at 100 percent, then no correction was applied.

EPA Ethics Assessment

Ms. Sherman reviewed the timeline of the AEATF study, which began with a protocol review by the HSRB in October 2009. Recruitment and subject enrollment began in April 2010 and field monitoring began in June 2010. The study was then stopped for 1 year before resuming subject monitoring in May 2011. Data analysis and reporting was completed in 2011, and the completed report was submitted to EPA in November 2011.

The subjects for this study were recruited by posting flyers at janitorial service providers identified through telephone directories and Chambers of Commerce. Of the 228 companies contacted, 34 agreed to post flyers. Advertisements also were placed in three Fresno County newspapers. Subjects obtained through both methods were interviewed by telephone to ascertain if they met the inclusion criteria, in which case they were scheduled for an informed consent meeting in person at Golden Pacific Laboratories. Ms. Sherman noted that the consent process was consistent with the protocol, equitable and free of coercion. No deviations were reported. During the consent meeting, potential subjects met with the study director or a Spanish-speaking researcher who explained the procedures, evaluated exclusion criteria, and gave the subjects consent documents with instructions to take the forms home to discuss with friends and family. After signing the consent form, the subject was enrolled in the study. Of the 42 people who came for consent interviews, 34 subjects were enrolled, and of those enrolled, 18 subjects were monitored. Regarding demographics, the study included 11 male and 7 female subjects, and 16 preferred that the process be conducted in English. The mean age was 46 years old and all had previous janitorial experience with a mean of 7.5 years.

Ms. Sherman explained that the study was put on hold after initial monitoring of four subjects in June 2010, some of whom expressed the desire to wear a respirator. The AEATF contacted EPA and IIRB and amended the protocol and consent form to offer subjects the option to wear a half-mask respirator. The protocol amendment and revised consent documents were approved by IIRB in May 2010 and four subjects, all of whom decided to use the respirator, were monitored in June 2010. Shortly thereafter, the CDPR asked for an additional review of the

respirator. The AEATF put the study on hold pending the outcome of the review. In a meeting in August 2010, EPA, sponsors and the study director decided to proceed with the study, giving subjects the option of wearing a respirator. CDPR approved the respirator documents and supported study resumption. Ultimately, all 18 monitored subjects chose to wear a respirator. During that hold, the original study director resigned and a new study director was named. The study resumed in spring 2011.

Monitoring was conducted with no incidents. Subjects were offered rest breaks, and six of the 18 subjects availed themselves of the opportunity. Some subjects asked for assistance with adjusting their respirator. No instances of sickness or injury were reported.

Ms. Sherman lauded the AEATF's responsiveness to EPA and HSRB protocol reviews, noting that all suggestions were taken into account. She explained that the investigators also complied with IIRB procedures and requirements. The initial protocol was reviewed by IIRB in August 2009. Four amendments, two of which were related to ethics, were approved by IIRB throughout the course of the study. The first amendment gave subjects the choice of wearing a respirator. The second amendment resulted in a revised procedure for removing subjects' socks during sample collection. The investigators revised the protocol to respect the subjects' preference to not remove their socks prior to removing the dosimeter. Ms. Sherman was pleased that the AEATF responded to the desires of the subject and modified the protocol accordingly.

Ethical deviations from the protocol include the enrollment of one subject who reported "fair health," but that subject was not monitored. Previous HSRB discussions about self-reported health as an study inclusion, initiated after the period of enrollment for this study, have led to development of an SOP that clarifies health status reporting, so this issue likely will not arise again. The ethics training certificate renewals of the original field study director and field coordinator were overdue when monitoring first began in 2010, but were current by the time monitoring resumed in 2011. Ms. Sherman noted no unreported deviations.

Ms. Sherman stated that the report and IIRB records were complete and well indexed, satisfying the requirements of 40 CFR §26.1303. The study also satisfied the following acceptance standards: 40 CFR §26.1703, which prohibits reliance on data involving intentional exposure of pregnant or nursing women or of children; 40 CFR §26.1705, which prohibits reliance on data unless EPA has adequate information to determine substantial compliance with subparts A through L for 40 CFR part 26; and FIRFA §12(a)(2)(P), which makes it unlawful to use a pesticide in human tests without fully informed and voluntary consent.

Ms. Sherman reported that all subjects were at least 18 years old, all females were tested for pregnancy, and pregnant or nursing women were excluded. Subjects were fully informed and their consent was fully voluntary without coercion. The protocol was faithfully executed and amended when needed; minor deviations did not compromise the safety or consent of the subjects. There were no noteworthy deficiencies in the ethical conduct of the research.

Ms. Sherman stated that the available information indicates the AEATF aerosol study was conducted in substantial compliance with 40 CFR part 26, subparts K and L.

Board Questions of Clarification—Ethics

Dr. Menikoff requested additional explanation about the nature of the CDPR concerns. Mr. Leighton deferred to the researchers and study sponsors to answer that question. Dr. Philpott invited Mr. William McCormick III, Mr. Robert Testman, and Ms. Megan Boatwright to respond to the questions. Mr. Testman replied that the primary concern of the CDPR was that although a procedure was in place to ensure that the subjects were qualified to wear a respirator, the CDPR wanted a respiratory protection plan document that included the subjects. The AEATF had one document that included researchers and staff and a separate procedure for the subjects. After the procedure was modified into a single document, the CDPR was satisfied because they wanted to ensure that subjects completely understood the procedure and compliance. The CDPR did not ask for protocol changes but rather clearly written documentation in one plan. Dr. Menikoff asked if the CDPR was worried about the respirator harming subjects or affecting the scientific results of the study. Mr. Testman stated that the CDPR did not have enough information at first to judge whether sufficient protections were in place, and they were not concerned about anything aside from better documentation. Ms. Sherman added that the CDPR asked for a review of the procedures in June 2010 and approval was granted in August 2010. Additional factors also influenced the 1 year study delay.

Dr. Popendorf asked if there was a minimum requirement for janitorial experience of the study subjects. Mr. Testman replied that there was a 1-year requirement and that all subjects were screened based on professional janitorial experience.

Dr. Popendorf asked for clarification about the sequence of the hotels monitored. Mr. Testman replied that the sites included kitchens and kitchenettes. The one site with the shorter average spray duration referred to earlier by Dr. Popendorf was a Hilton hotel with a kitchenette design. The application likely went faster because it was a bigger layout with a full shower and no bathtub, so the subjects were able to cover more square footage much quicker. Additionally, the rooms were closer together at the Hilton hotel. Subjects took longer to move from room to room at the Piccadilly hotel site. Another possible explanation is that the researchers improved over time and did not impede the progress of the subjects at the later sites.

Dr. Popendorf noted that it appeared that all of the subjects were covered by the OSHA respiratory protection plan along with the researchers and staff. Mr. Testman said that the CPDR had wanted everyone addressed in the same written plan and the AEATF had to comply with OSHA guidelines, although it was unclear why voluntary subjects would be covered under the OSHA plan because OSHA only regulates employees.

Dr. Philpott summarized that it sounded like CPDR wanted to ensure that subjects were adequately informed and knew how to use the respirator, noting that the use of a respirator was not otherwise required for use of this disinfecting product.

Dr. George Fernandez asked how the hotels were selected. Mr. Testman explained that the original list was selected from the telephone book and other sources. The hotels were then categorized by the presence of a kitchen into groups of “hotel only,” “kitchenette,” or “kitchen.” The investigators chose one hotel from each category through use of a randomization program. The hotel was then asked if they would like to participate in the study. Mr. Testman noted that there were more potential hotels without kitchens than ones with full kitchens. Dr. Fernandez asked whether these hotels were treated as random and thus could be used to make inferences about

similar establishments. Mr. Testman affirmed that the study protocol was designed specifically for hotels. Mr. Leighton noted that they had originally considered using unoccupied buildings, but they settled on using hotels because of the large number of available rooms to treat.

Dr. Fernandez questioned whether the findings would be limited to a hotel environment, noting that households may have open windows and more air circulation. He commented that environmental conditions can influence the study approach. Mr. Leighton explained that the study measured 0.6 to 2 air exchanges in the hotels and noted that it would be better to have low air exchanges to make a conservative estimate of exposure.

Dr. Johnson commented that the study design had been discussed in detail, including what results can be concluded based on these data. He noted that the statisticians are responsible for helping EPA realize that some of the inferences are not based on statistical conjecture but rather expertise and knowledge of the situation. Dr. Johnson accepted the limits of the data.

Mr. McCormick clarified that the commercial Clorox solutions are supplied in 19-ounce cans compared to the 13-ounce consumer can. Dr. Popendorf noticed that the reported averages of the flow rates of two batches of cans differed by 20 percent. He questioned if that difference was statistically significant and if there was any information regarding how variable flow rates are between cans. Mr. Testman replied that there was no information on the variability of flow rates, but noted that the test was designed by the AEATF and was not using an SOP supplied by Clorox. The AEATF performed that calculation to understand how fast the product discharges to ensure it occurred at a reasonable rate. Mr. Leighton referred the HSRB to the original protocol rationale for the study, which described a test of the spray characteristics for 18 different products. There was no protocol for that test. Rather, it was used to inform the product selection criteria.

Dr. Philpott asked the study sponsors to explain why the subject who self-reported “fair health” was enrolled despite the fact that he did not meet the inclusion criteria. Mr. Testman speculated that the original study director may have been looking at multiple criteria of health, the self-reported value being only part of the decision. He noted that another individual who self-reported “good health” was excluded for other health reasons. Dr. Philpott asserted that it would be useful to clarify the exact method of determining health in future protocols.

Dr. Popendorf asked whether the first four subjects were monitored by the same field personnel, and Mr. Testman assured him that they were.

Mr. Testman thanked the Board for their remarks and expressed appreciation for their time and effort in reviewing the studies.

Public Comments

Dr. Philpott called for public comments on the AEATF II completed study; no public comments were presented.

Charge Questions

Ms. Sherman read the charge questions into the record:

- Was the research reported in the AEATF II completed aerosol study report 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 professional janitorial workers who apply liquid antimicrobial pesticide products to indoor surfaces using pressurized aerosol cans?

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

Board Science Review

Dr. Philpott asked Dr. Popendorf, as Lead Science Discussant, to address the first two charge questions. Dr. Popendorf first disclosed that he had stayed at one of the hotels in the study. He began his analysis by stating that the study was done thoroughly, the information provided was helpful and detailed, and the individual data appear reliable. When he looked for patterns within the data, he found some trends that were not explained. Dr. Popendorf noted that the diversity of subjects and study settings makes the study strong. He mentioned a few limitations of the study. Although the field notes were very thorough, he noticed that subject AE4 had been given instructions to "lighten up" his application. This reflects two points of relevance. First, the protocols stated that subjects were to apply the product as they normally do, but in this case the researcher intervened. This may have been a worthwhile activity to prevent harm, but the situation was not documented as a deviation. Dr. Popendorf remarked that there were some interesting outliers, one of which was subject AE18. Dr. Popendorf outlined reasons to consider that data point an outlier, but he emphasized that he was not suggesting that be done. Dr. Popendorf recommended that the data be kept in the analysis for the sake of robustness, although that subject had exposure levels much higher than the average subject. He also mentioned that future protocols should define more precisely when intervention is appropriate and when a subject should be considered an outlier. For example, if someone was very meticulous, they could have no exposure.

Dr. Popendorf questioned how the values were calculated for ventilation in air changes per hour. He had attempted to replicate the results using various calculations of room volume and flow rates but could not duplicate the reported values. The second cluster had reported 100 percent recirculated air, and Dr. Popendorf would like to see that clarified. He noted that the ventilation calculation could be viewed from a different perspective of the time for one air exchange. If subjects spend a few minutes in each room, the air exchange rate will not make much of a difference. Dr. Popendorf summarized that although there may be problems with the way ventilation has been calculated and recorded, he does not think those calculations will significantly affect the results.

Dr. Popendorf's final comment was related to differences between the first four subjects and the remaining 14 that were monitored after the study interruption. He noted that the discharge rates on the cans were different between the two sets, and the percentage of product also was different. The measurement of total aerosols versus particles less than 10 µm were dissimilar between the two sets, as were RPS and OVS measurements. In his pattern analysis, Dr. Popendorf noted that an increase in the flow rate of the nebulizer would result in a smaller particle size that is inhaled less. The RPS contained a fraction of 50 percent in the 10 µm range, which was higher in the first four subjects. He noted the possibility that the flow rate differences were real and may not constitute a limitation, but rather increase the variability of the data. Dr. Popendorf suggested that

the aerosol flow rate deserves consideration because of the 20 percent difference between sets. He noted that his comments did not indicate major problems and were designed to make the study more robust, more useful and more reliably extrapolated to other settings.

Dr. Lebowitz, Associate Discussant for this protocol, stated that he agreed with Dr. Popendorf on many of the comments. He suggested combining dermal and inhalation exposures to determine the actual exposure levels. Dr. Lebowitz was pleased to see that the EPA analysis adjusted for fortified samples. However, he noted that some questions of clarification were not answered, including whether a slope of 1.5 indicates true proportionality. This needs to be evaluated by EPA to improve upon future study protocols. Dr. Lebowitz concluded by thanking the Board and EPA for his 6 years of service.

Dr. Johnson suggested that the HSRB discuss the term "proportional." He noted that a deviation from a slope of 1, such as 1.2 or 1.3, is still proportional although the term is not applied unless the slope approximates exactly 1. Mr. Leighton agreed that the term proportional would be excluded from future reports.

Dr. Johnson reiterated that the earlier questions regarding the EPA Science Review figures could have been prevented by maintaining one scale or the other, either log-log or exposure versus AaiH. He suggested additional discussion about the figures and what can be interpreted from them, not for the purposes of asking EPA to rewrite the review, but to clarify the impact on other reviews. Dr. Johnson suggested including the models in the body of the EPA Science Review rather than the appendix. Dr. Johnson responded affirmatively to both charge questions.

Dr. Philpott solicited further discussion on a topic raised by Mr. Leighton in the Agency's Science Review. Specifically, was it was proper to correct the data from the RPS back to OVS, or should the two data sets should be considered separately? Mr. Leighton clarified that they have not yet applied the correction and welcome the Board's input. Dr. Lebowitz responded that because 10 µm particles were more important than 100 µm particles, he thought that the RPS results would be more useful in terms of inhaled dose than the OVS results. Dr. Popendorf agreed with Dr. Lebowitz, noting that literature suggests a correction of 1.5 to 1.8 for respiration. The 10 µm particle differences were not large in the RPS measurements, especially within the first four replicates, which were nearly identical. Comparisons between RPS and OVS were very similar in the first four samples, but the other 14 varied substantially up to 76 percent. He would not recommend applying a large correction to the first four subjects; at most, a correction factor of 1.3 is needed.

Dr. Young expressed appreciation for the effort that went into the analyses and noted that each review gets better. She pointed out that Dr. Johnson is fine-tuning the analyses rather than suggesting the existence of major issues. In Dr. Young's opinion, the CI of the slope of 1.5 covers 1, so she is not concerned with calling the relationship between inhalation exposure and AaiH proportional. If a CI does not cover 1, the analysis may need to be handled differently.

Dr. Philpott summarized the Board's consensus opinion. He stated that the research reported is faithful to the design, and EPA has characterized many of the limitations on using the data to estimate exposure of professional workers. He noted a few caveats, such as the issue of variability introduced by Dr. Johnson. Dr. Philpott emphasized the importance of being cognizant of the limitations to general applicability of a janitorial worker to a consumer. He repeated Dr. Popendorf's observation of differences between the first set of four subjects and the rest, which were attributed to the study's delay. In particular, differences in the discharge rate of the aerosol

cans could affect inhalation data. Dr. Philpott entreated EPA and the sponsors to consider differences between these two groups in the analysis. The Board considers the RPS data to be more useful than the OVS data and should be treated as a more representative value of the amount of product inhaled.

Dr. Young emphasized that coefficients larger than 1 require clarification. In particular, slopes of 1.5 where the CI does not cover 1 are of concern and proportionality should not be assumed. Dr. Popendorf requested that the report also include clarification that possible ventilation calculation errors might not affect the results, to which Dr. Philpott noted that EPA is now aware of that limitation and the HSRB will clearly detail the rationale for this recommendation in its report.

Board Ethics Review

Dr. Philpott noted that Dr. Popendorf had left the meeting but the Board was still had quorum. Dr. Philpott asked Dr. Menikoff, as Ethics Lead Discussant, to discuss whether 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. Menikoff agreed that the study was conducted with substantial compliance. He thanked Ms. Sherman for the thorough analysis and noted that EPA researchers continue to refine their studies according to HSRB review. Dr. Menikoff commended the good study design and noted that the minimal deviations were largely inconsequential. Recruitment lacked coercion, and pregnant and nursing women were excluded from the study. Regarding the voluntary use of respirators, he commended the researchers for making the effort to add an additional element of protection that was not required. Dr. Menikoff agreed that the self-reported condition of “fair health” was not the best estimate for excluding an individual from the study. He noted that those criteria have been redesigned and will be applied to future studies.

Dr. Philpott, Associate Discussant for this protocol, also commended Ms. Sherman for her ethics review given the challenges of the study interruption, amendments and reported deviations. Her thorough analysis facilitated the Board’s review. He agreed with Dr. Menikoff that the sponsor and investigator could not be faulted for enrolling a person with reported “fair health” because the subject was enrolled prior to HSRB review of the issue. Although not relevant to the charge question, the issue of self-reported health will need to be clarified in the future.

Dr. Johnson had one more remark regarding the science of the study. He expressed surprise at the consistency of the quantile plots given the amount of scripting in the studies. Even with all of the variables, the results still look like random sampling and are statistically robust.

Dr. Philpott stated that the general Board consensus was that the answer to the ethics charge question is “yes” and that the Board is in agreement that the available information supports the determination that the study was conducted in substantial compliance with subparts K through L of 40 CFR part 26. With that determination, the Board review of the two agenda items was concluded.

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

Dr. Philpott noted that there was no update regarding the working group's analysis of the return of individual research results. Dr. Lux mentioned that his office is available to provide guidance on areas such as the reporting of results, and the Agency is welcome to contact him.

Adjournment

Dr. Philpott stated that it has been a privilege to have worked with the Board, and he acknowledged Mr. Downing's efforts as DFO. Dr. Philpott also stated that it has been a pleasure to work with all of the Board members, and he is grateful for the opportunity to have become colleagues. He acknowledged the efforts of Drs. Chambers and Parkin, who served as his vice-chairs during the past 3 years. He thanked Ms. Susan Podziba, an EPA contractor, for providing support in facilitating the HSRB meetings. Dr. Philpott thanked the EPA staff of Drs. Lux and Cohen, Ms. Sherman, and Mr. Evans, Mr. Jordan and Mr. Leighton. He also expressed gratitude to the sponsors for being responsive to the Board's concerns. Dr. Philpott concluded that the change seen over the past 6 years of the Board's existence in terms of quality of research has been remarkable.

Mr. Downing announced that the April 2012 meeting was cancelled due to a lack of discussion topics. The date and times of the next meeting will be announced in the *Federal Register* and posted on the HSRB website. Mr. Downing adjourned the meeting at 3:51 PM.

Respectfully submitted:

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

Certified to be true by:

Sean Philpott, Ph.D., M.S. Bioethics
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	HSRB Members
Attachment B	Federal Register Notice Announcing Meeting
Attachment C	Meeting Agenda

Attachment A

EPA HUMAN STUDIES REVIEW BOARD MEMBERS

Chair

*+Sean Philpott, Ph.D., M.Bioethics — Term: 3/27/2006–8/31/2012
Director, Research Ethics
The Bioethics Program
Union Graduate College–Mt. Sinai School of Medicine
Schenectady, NY

Vice Chair

*+Rebecca T. Parkin, Ph.D., M.P.H. — Term: 10/1/2007–8/31/2013
Professorial Lecturer (EOH)
School of Public Health and Health Services
The George Washington University
Lake Frederick, VA

Members

*+Janice Chambers, Ph.D., D.A.B.T. — Term: 3/27/2006–8/31/2012
William L. Giles Distinguished Professor
Director, Center for Environmental Health Sciences
College of Veterinary Medicine
Mississippi State University
Mississippi State, MS

*+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

*Vanessa Northington Gamble, M.D., Ph.D. — Term: 10/19/2009–10/31/2012
University Professor of Medical Humanities
Gelman Library
The George Washington University
Washington, DC

*+Sidney Green, Jr., Ph.D., Fellow, ATS — Term: 10/19/2009–10/31/2012
Department of Pharmacology
Howard University College of Medicine
Howard University
Washington, DC

*+Jewell H. Halanych, M.D. Term: 11/14/2011–8/31/2014
Assistant Professor
Department of Medicine
Division of Preventative Medicine
University of Alabama at Birmingham
Birmingham, AL

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

*^Michael D. Lebowitz, Ph.D., FCCP Term: 3/27/2006–8/31/2012
Retired Professor of Public Health
(Epidemiology) and Medicine Research Professor of Medicine
University of Arizona
Tucson, AZ

*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

#Jerry A. Menikoff, M.D. Term: 3/27/2006–8/31/2012
Director, Office for Human Research Protections
Office of the Secretary
Department of Health and Human Services
Rockville, MD

*+William J. Popendorf, Ph.D. Term: 10/19/2009–10/31/2012
Professor Emeritus
Department of Biology
Utah State University
Logan, UT

*Leonard Ritter, Ph.D. Term: 11/14/2011–8/31/2014
Professor Emeritus (Toxicology)
School of Environmental Sciences
University of Guelph
Guelph, Ontario, Canada

*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

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

*+Linda J. Young, Ph.D. Term: 3/28/2008–8/31/2012
Professor and Associate Chair
Department of Statistics
Institute of Food and Agricultural Sciences
University of Florida
Gainesville, FL

*Special Government Employee (SGE)
^ Present via telephone January 26, 2012
+ Present on January 26, 2012
# Present for Session 2 on January 26, 2012

Attachment B

Federal Register Notice Announcing Meeting

[Federal Register Volume 76, Number 248 (Tuesday, December 27, 2011)]
[Notices]
[Pages 80938-80940]
From the Federal Register Online via the Government Printing Office [www.gpo.gov]
[FR Doc No: 2011-33156]

ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-ORD-2011-0954; FRL-9611-6]

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

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

ACTION: Notice.

SUMMARY: The U.S. Environmental Protection Agency (EPA) Office of the Science Advisor (OSA) announces a public meeting of the Human Studies Review Board (HSRB) to advise the Agency on EPA's scientific and ethical reviews of research with human subjects.

DATES: This public meeting will be held on January 26, 2012, from approximately 9 a.m. to approximately 5:30 p.m. Eastern Time. Comments may

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be submitted on or before Thursday, January 19, 2012.

ADDRESSES: Submit your written comments, identified by Docket ID No. EPA-HQ-ORD-2011-0954, 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- 2011-0954. 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) 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.

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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 26, 2012, EPA's Human Studies Review Board will consider scientific and ethical issues surrounding these topics:

a. A new scenario design and associated protocol from the Agricultural Handler Exposure Task Force (AHETF) describing proposed research to measure dermal and inhalation exposure to workers who mix, load and apply liquid pesticides with powered handgun equipment. EPA requests the advice of the HSRB concerning whether, if it is revised as suggested in EPA's review and if it is performed as described, this research is likely to generate scientifically reliable data, useful for assessing the exposure of those who mix, load and apply liquid pesticides with powered handgun equipment, and to meet the applicable requirements of 40 CFR part 26, subparts K and L.

b. The report of a completed scenario monograph and 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 applied a liquid antimicrobial pesticide

product for indoor surface disinfecting using a pressurized aerosol can. The EPA seeks the advice of the HSRB on the scientific soundness of this completed research and on its appropriateness for use in estimating the exposure of professional janitorial workers who apply liquid antimicrobial pesticide products to indoor surfaces using pressurized aerosol cans, and 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 19, 2011.
Paul T. Anastas
EPA Science Advisor
[FR Doc. 2011-33156 Filed 12-23-11; 8:45 am]
BILLING CODE 6560-50-P

Attachment C

U.S. ENVIRONMENTAL PROTECTION AGENCY
HUMAN STUDIES REVIEW BOARD
JANUARY 2012 PUBLIC MEETING AGENDA

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

Thursday, January 26, 2012

HSRB Website: http://www.epa.gov/osa/hsrb/
Docket Telephone: (202) 566-1752
Docket Number: EPA–HQ–ORD–2011–0954

9:45 AM* **Convene Public Meeting** – Jim Downing (Designated Federal Officer, EPA Human Studies Review Board, Office of the Science Advisor)
Introduction of Board Members – Sean Philpott, Ph.D. (HSRB Chair)
Welcome – Warren Lux, M.D. (Director, Program in Human Research Ethics, Office of the Science Advisor, EPA)
Follow-up on Previous HSRB Recommendations – Mr. William Jordan (Office of Pesticide Programs [OPP], Office of Chemical Safety and Pollution Prevention, EPA)

Session 1: **A new scenario design and associated protocol from the Agricultural Handler Exposure Task Force (AHETF) describing proposed research to measure dermal and inhalation exposure to workers who mix, load and apply liquid pesticides with powered handgun equipment.**

10:00 AM **EPA Science Review** – Mr. Jeff Evans (OPP, EPA)
10:25 AM **Board Questions of Clarification** – Sean Philpott, Ph.D. (HSRB Chair), EPA, Principal Investigator/Sponsor
10:55 AM **EPA Ethics Assessment** – Ms. Kelly Sherman (OPP, EPA)
11:15 AM **Board Questions of Clarification** – Sean Philpott, Ph.D. (HSRB Chair), EPA, Principal Investigator/Sponsor
11:35 AM **Public Comments**
11:50 AM **Board Discussion**

Charge to the Board – Science:

- Is the research likely to generate scientifically reliable data, useful for assessing the exposure of workers mixing, loading and applying pesticides in managed horticultural facilities using powered handgun equipment?

Charge to the Board – Ethics:

- Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

12:30 PM* Lunch

Session 2: A completed scenario monograph and 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 applied a liquid antimicrobial pesticide product for indoor surface disinfecting using a pressurized aerosol can.

1:30 PM* EPA Science Review – Mr. Tim Leighton (OPP, EPA) and Jonathan Cohen, Ph.D. (ICF International)
1:55 PM Board Questions of Clarification – Sean Philpott, Ph.D. (HSRB Chair), EPA, Principal Investigator/Sponsor
2:20 PM EPA Ethics Assessment – Ms. Kelly Sherman (OPP, EPA)
2:45 PM Board Questions of Clarification – Sean Philpott, Ph.D. (HSRB Chair), EPA, Principal Investigator/Sponsor
3:10 PM Public Comments
3:25 PM Board Discussion

Charge to the Board – Science:

Was the research reported in the AEATF II completed aerosol study report 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 professional janitorial workers who apply liquid antimicrobial pesticide products to indoor surfaces using pressurized aerosol cans?

Charge to the Board – Ethics:

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

4:20 PM An update from the Work Group on Return of Individual Research Results

4:30 PM Adjournment

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