Minutes of the
United States Environmental Protection Agency (EPA)
Human Studies Review Board (HSRB)
January 26, 2011 Public Meeting
Docket Number: EPA-HQ-ORD-2010-0970
HSRB Web Site: http://www.epa.gov/osa/hsrb

Committee Members: (See EPA HSRB Members list – Attachment A)

Date and Time: Wednesday, January 26, 2011, 9:15 AM – 5:30 PM
(See *Federal Register* Notices – Attachment B)

Location: EPA, One Potomac Yard (South Bldg.), 2777 S. Crystal Drive, Arlington, VA 22202

Purpose: The EPA Human Studies Review Board 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:	Janice Chambers, Ph.D., D.A.B.T.
Board Members:	George C.J. Fernandez, Ph.D.
	Vanessa Northington Gamble, M.D., Ph.D.
	Sidney Green, Jr., Ph.D., Fellow, ATS
	Dallas E. Johnson, Ph.D.
	Michael D. Lebowitz, Ph.D., FCCP
	José E. Manautou, Ph.D.
	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 in these minutes.

Meeting Administrative Procedures

Mr. Jim Downing (Designated Federal Officer [DFO], Human Studies Review Board [HSRB or Board], Office of the Science Advisor [OSA], U.S. Environmental Protection Agency [EPA or Agency]) convened the meeting and welcomed Board members, EPA colleagues, and members of the public. He thanked Board members for their work in preparing for the deliberations that would follow.

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 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 the OSA and the Office of the General Counsel, Mr. Downing has reviewed the reports to ensure that all ethics requirements are met.

He informed members that there were two challenging discussion items on the agenda for the meeting, and that agenda times are approximate. Copies of the meeting materials and public comments will be available on www.regulations.gov under docket number EPA-HQ-ORD-2010-0970. Following the presentations, time has been scheduled for questions of clarification to EPA staff and the principal investigator and sponsors of the studies discussed. A public comment period will be maintained and remarks must be limited to 5 minutes. During Board discussions, if members require clarification from the public, they may request such information through the Chair or DFO. All background materials for the meeting will be available in the public docket and most also are available on the HSRB Web site. 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 as a 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 through the *Federal Register*. Mr. Downing welcomed Dr. Warren Lux (Director of the Program in Human Research Ethics, OSA, EPA) who would offer the Board welcoming remarks.

Welcoming Remarks

Dr. Lux welcomed all in attendance on behalf of EPA's Program in Human Research Ethics and Dr. Paul Anastas, EPA Science Advisor, and expressed his appreciation that the HSRB was among the program's components. He noted that the Board's expertise and thoroughness had been critical to the program's success, and that its members had contributed significantly to the scientific and ethical standards adopted by the regulated community. He thanked his colleagues in EPA's Office of Pesticide Programs (OPP) for their preparation and commitment to HSRB activities, and the regulated community and the public for their engagement with the Board. He wished the Board a successful and productive meeting, and turned the meeting over to Dr. Sean Philpott, HSRB Chair.

Introduction and Identification of Board Members

Dr. Sean Philpott welcomed members of the public to the meeting and thanked the Agency and Board members for their service. He asked Board members to introduce themselves and welcomed Mr. William Jordan (OPP, EPA).

EPA Follow-up on Previous HSRB Recommendations

Mr. Jordan added his welcome and thanks. He noted that at the previous HSRB meeting in October 2010, the Board examined the first major completed study on human exposure for

people handling pesticides, Antimicrobial Exposure Assessment Task Force II (AEATF–II) Report AEA03, Dermal and Inhalation Monitoring of Workers Mopping Floors with an Antimicrobial Product.

The HSRB offered recommendations regarding the statistical analyses performed, and Dr. Jonathan Cohen, a consultant to EPA, performed additional statistical analyses that confirmed and supported the conclusions reached by EPA. Based on the additional analysis and the Board's recommendations, EPA intends to use the data from the study to assess future applications for antimicrobial products that involve application through mopping; none are pending at this time.

Protocol reviews conducted at the October 2010 HSRB meeting included that of the *No Mas 003* Field Efficacy Test of Para-menthane-3,8-diol (PMD**)** and Lemongrass Oil-Based Repellent Against Mosquitoes. The Board offered comments regarding the statistical analysis of the data set that would be generated by the study, and the study director, Dr. Scott Carroll of Carroll-Loye Biological Research, has proposed a Weibull distribution for analysis of the data.

The other two protocol reviews conducted in October 2010 were both from the Agricultural Handler Exposure Task Force **(**AHETF): AHE-400, New Scenario Design and Protocol for Applicators Using Backpack Sprayers or Handgun Sprayers for Rights of Way, and AHE-120, Revised Scenario Design and Protocol for Exposure Monitoring of Workers during Mixing and Loading of Pesticide Products in Water Soluble Packets. The Board found both protocols to be scientifically and ethically acceptable. The AHETF has made revisions and submitted protocols to Independent Institutional Review Board, Inc. (IIRB), which approved them. The recruiting process for AHE-400 will begin on February 1, 2011, and recruitment for AHE-120 is scheduled to begin in March 2011. The studies are expected to be completed this summer, and the Board will likely review the results in October 2011 or January 2012.

Mr. Jordan also informed the Board that EPA Administrator Lisa Jackson signed a *Federal Register* notice of proposed rulemaking on January 18, 2011, for the proposed revisions to EPA's "Rule on Protections for Subjects in Human Research Involving Pesticides." It will be published in early February 2011, and will include a 60-day public comment period. The content of the proposed amendments matches what has previously been described to the Board. The proposed changes serve primarily to codify practices that EPA has been following in its reviews, and ensure that the research performed under this rule meets high ethical standards and is scientifically sound. Mr. Jordan does not expect the proposed rule to generate much controversy.

Session 1: AHETF Report of a Completed Scenario Monograph and Study Reports of Five Field Studies Measuring the Dermal and Inhalation Exposure of Workers Applying Liquid Spray Pesticides to Tree or Trellis Crops Using Closed Cab Airblast Equipment

Background

Ms. Kelly Sherman (OPP, EPA) noted that the closed cab airblast applicator study is the first AHETF completed study and monograph to be reviewed by the HSRB. Questions for completed studies differ from those for protocols, and Ms. Sherman explained that the Board

should consider if: the proposal was appropriately amended after review by EPA and the HSRB; it was executed faithfully; results achieved objectives; and it was conducted ethically.

The closed cab airblast applicator study involved five separate field studies in different locations with varying crops: AHE55, AHE56, AHE57, AHE58, and AHE59. The study monitored 24 subjects' dermal and inhalation exposures during pesticide application with closed cab airblast equipment. The HSRB reviewed protocols for these studies in June and October 2008.

EPA Science Assessment

Mr. Matthew Crowley (OPP, EPA) thanked colleague Mr. Bayazid Sarkar (OPP, EPA) for his statistical analyses of the study data. The research objectives were to collect robust dermal and inhalation exposure data of workers applying liquid spray pesticides with closed cab airblast equipment for use in regulatory assessments of pesticides. This was a study designed to capture the variability of exposure encountered by agricultural workers. The primary objective was to determine the amount of dermal exposure, and the secondary objective was to determine whether the relationship between the amount of active ingredient handled (AaiH) and exposure was proportional or independent. The AHETF previously had demonstrated that a sample size of 25 (5 x 5 configuration) could satisfy the objectives; because of logistical considerations as well as necessary scripting, however, true random sampling was not feasible. The AHETF targeted certain locations and worked with EPA to ensure that there was diversity among workers and different AaiH. The task force was responsive to HSRB comments on the study protocol.

The AHETF was able to collect data from distinct geographical locations across the United States. Only one location per EPA growing region was monitored. Five subjects were monitored in each location except for one, in which four were monitored; this occurred because no monitor was available for the fifth worker. All subjects were male except for one female. Their work experience varied, as did the equipment, but all vehicles used had functioning windows and air conditioning. The goal was for the task force to configure each of the subjects within a study into one of five target ranges of AaiH. In most cases, this was successful. Dermal exposure was monitored by hand wash, face and neck wipe, and whole body dosimeter (WBD), and inhalation exposure was monitored by air pump and Occupational Safety and Health Administration Versatile Sampler (OVS) tubes.

Several deviations from the protocol occurred, but in EPA's opinion, none undermined or compromised the exposure results. In some cases, EPA suggested that the protocol be edited in the future to account for some of the deviations, such as with the requirement of 4 hours of spray time versus 4 hours of exposure monitoring time. The studies included Quality Assurance Statements, and the AHETF Quality Assurance Unit ensures that studies follow EPA Good Laboratory Practice Standards. Both negative controls (blanks) and positive controls (spikes) were included in the study. Some residues were detected in the field that should be discussed in the study reports. Exposure measurements represent workers wearing long-sleeved shirts, pants, chemical-resistant gloves, shoes/socks, and no respirator. All measurements were adjusted by average recovery of corresponding field fortification matrix and level. Left-censored data were present mainly in the face/neck wipes and OVS back sections results. Based on

recommendations from previous HSRB meetings, if the measured contribution from hands and face/neck represents between 20 percent and 60 percent of the total, measurements are to be adjusted upward by 2, or a validation study supporting the method's efficiency must be provided. This is referred to as Method Efficiency Adjusted (MEA) or Method Efficiency Corrected (MEC) data.

Dermal exposure ranged from 10 to 3,000 micrograms (µg). Inhalation exposure ranged from 0.1 to 67 µg. For inhalation, in one study, the worker was monitored, but the amount of time the air pump was operating was not recorded, so the sample size was 23. The AHETF characterized the estimates of exposures normalized by AaiH by empirical estimates, simple random sample, and mixed model method; the latter is the most appropriate for the study. Both the dermal and inhalation unit exposures (µg exposure per pound [lb] active ingredient [ai] handled) follow a log normal distribution. Statistical analysis demonstrates that the primary objective benchmark was met, and no additional monitoring is necessary. In terms of the secondary objective, in routine EPA assessments of handler exposure, exposure is predicted from AaiH, which assumes the two are proportional. The mixed model regression slope results show that this is the case for inhalation exposure, but show that dermal exposure is independent from AaiH. Therefore, the secondary benchmark was met for inhalation exposure but not dermal exposure. Considering the inconclusive results on dermal exposure, EPA performed additional analyses that found a stronger relationship between dermal exposure and handler entrances into and exits from the cab than AaiH. Field observations showed high exposures potentially caused by incidental contacts, such as brushing against foliage or touching with bear hands exterior surfaces that may have residue on them. Incidental contacts may correlate with the number of times a handler enters or exits the vehicle.

In conclusion, EPA agreed that the research design was acceptable despite its limitations. The selection of the workers was randomized to the extent possible. The data are recommended for use in regulatory assessments with AaiH normalization as a default condition; they should not be used, however, for assessments of high volatility chemicals.

EPA Ethics Assessment

Ms. Sherman explained that recruiting was conducted following a three-phase process that is outlined in the protocols, and in general the process in the standard operating procedures (SOPs) was followed. The initial recruitment list was generated from public lists and varied across the five studies from several hundred to several thousand. This list was narrowed using acreage size and other qualifying questions; the study director then spoke to those who were interested and could participate. There was one reported deviation in the Georgia pecan study. Because of a research delay caused by a tropical storm, several of the growers initially planning to participate in the study were either no longer available or willing to participate. Two referred growers ultimately became study subjects, but EPA determined that this did not compromise the recruiting process.

Twenty-four subjects were monitored, including one female who was not pregnant. Most of the subjects preferred to conduct their consent process in English rather than Spanish, but there were three who chose Spanish, and one subject in Florida who self-identified as a non-

reader used a witness for the consent process. There was diversity in age (20 to 70 years old) and level of experience (3 to 50 years). In two cases, the subjects reported a surprisingly large amount of experience in comparison to their ages, so those values may be questionable. All of the subjects except for one requested to have their exposure results provided to them at the end of the study. None of the subjects withdrew, and none were removed from participation by the task force.

Exposure monitoring was conducted without incident, and no adverse events were reported. Initial protocols of all of the studies were reviewed by IIRB. Subsequent amendments and deviations were reviewed under expedited procedures. Eight amendments were approved by IIRB across the five studies, and 13 reported deviations were reviewed and acknowledged by IIRB.

A large number of ethics issues were raised by the HSRB and EPA in terms of the study protocols, and in general, the researchers responded to all of the comments. Changes were implemented at different times: some before the first two studies were conducted, some before the next group of three studies, and some have been implemented for future protocols.

Additionally, there were a number of protocol amendments; each of the five studies was amended at least once to address HSRB and EPA comments, and there were additional amendments to the three studies conducted in 2009 (AHE57, 58, 59). An amendment to study AHE59 involved the addition of two new carbaryl products to the protocol. When it became close to the time to conduct the monitoring, the AHETF learned that there were two eligible growers who wanted to use two products containing carbaryl that were not among those that had been approved previously. EPA approved of the amendment, and it also was approved by IIRB, but not through a formal protocol amendment. EPA did not consider this an ethics violation.

Key deviations reported across the five studies included, in study AHE56, a subject signing the informed consent form (ICF) after putting on the inner dosimeter. It was reported that he had given oral consent before donning the dosimeter, and he signed the ICF shortly after dressing. This was not in accordance with the protocol, but EPA did not consider it an ethics violation.

There were 13 unreported deviations in the study report, including the fact that minimum spray time was not reached, and a subject contacted contaminated surfaces while not wearing gloves. In this case, he was not reminded to wear gloves by the monitor, and the study director was not informed. Observations were made of subjects exiting the cab while not wearing gloves in three of the studies. These deviations were compared to the Worker Protection Standard (WPS) that provides personal protective equipment (PPE) requirements for individuals working inside enclosed cabs. The WPS states that PPE required on the product label must be worn “if it is necessary to exit the cab and contact pesticide-treated surfaces in the treated area.” In these cases, the surfaces contacted by workers not wearing gloves may have been contaminated but were not treated, and therefore, the deviation did not constitute a WPS violation. The protocol for the study, however, required a higher standard, and the failures to remind the worker to wear gloves and to report the deviation to the study director are violations of SOPs. In addition, these protocol and SOP deviations should have been reported promptly to IIRB. Ms. Sherman

determined that the deviations did not constitute an ethical violation because there was no intent to harm the subject, the safety of the subjects was not jeopardized, there was no violation of product labels or the WPS, and investigators were not sufficiently informed about what type of behavior should have required a warning. She also concluded that there was no regulatory violation because of these deviations.

The study overall was complete and well-documented, and requirements of ethical documentation at 40 Code of Federal Regulations (CFR) §26.1303 were satisfied. Ms. Sherman's findings were that the relevant substantive acceptance standards were met, and she concluded that available information indicates that the AHETF closed cab airblast applicator studies (AHE55, 56, 57, 58, 59) were conducted in substantial compliance with subparts K and L of 40 CFR part 26.

Board Questions of Clarification

Dr. Michael Lebowitz asked why the California study was so different in terms of both exceedance of the upper limits of the strata, the design, and also the WBD field fortification samples. Mr. Crowley responded that the task force may have something to add about the California study; it is correct that it did have the most deviation from the targets. Variability in field fortification existed across all of the studies. Dr. Lebowitz noted that he had seen the data on wind speed, temperature, and humidity, but had not seen any analysis of the effect of any of those factors in the exposure assessments. Mr. Crowley replied that these analyses were not conducted, but EPA might be able to determine that information from the data.

Dr. Linda Young stated that the assumption of normalization is that proportionality holds. What would be the consequences from the regulatory standpoint if that assumption is made and it is incorrect? Would it be protective of humans? Mr. Crowley answered that the slopes of the line were less than one. If the slope is assumed to be one, it would indicate that exposure is being overestimated. There is not a chance that the exposure would be underestimated.

Dr. Dallas Johnson commented that in the report and presentation, it was mentioned that 80 percent power was used, and asked if there was always a 95 percent confidence interval (CI). Mr. Crowley confirmed that this was the case.

Dr. William Popendorf noted that if proportionality is assumed but is not present, this would overprotect for high amounts of use but underprotect for low amounts of use. Mr. Crowley replied that the method applied in EPA's assessments generally is to use maximum application rates, with amounts treated that would be considered at the high end of the range. He added, however, that Dr. Popendorf was correct in his assumption.

Dr. Young stated that it was not quite clear how the assessment of 80 percent power was conducted. Mr. Crowley answered that he would defer to Mr. Sarkar on this issue, but that the AHETF's governing document had a description stating that if the 95 percent CI slope had the width of 1.4, it would correspond to a power of 80 percent. Mr. Sarkar agreed that more detail was presented in the governing document, but a CI of 1.4 translates to 80 percent power. Dr. Philpott asked that the governing document containing the information be provided to Drs.

Young and Johnson, and then be addressed in the discussion if there are concerns.

Dr. José Manautou noticed in the reports that with the data for both dermal and inhalation exposure (on slides 24 through 26), density of the foliage varies from one site to another. The Florida site is the most consistent. He asked if the Agency assessed whether the foliage density impacts the total outcome of inhalation or dermal exposure. If the foliage is less dense, perhaps more of the chemical will stay in the air and come into contact with the workers. Mr. Crowley commented that this was a good observation; EPA can look at the different variables and think about how they could affect exposure. Analysis on foliage density was not conducted, but could be to the extent that the data allow. The researchers did not target certain levels of density, so when EPA uses the data, numbers will be used without consideration of that as a specific variable.

Dr. George Fernandez questioned why the 1.645 value was used for the upper CI computation. Mr. Crowley confirmed that Dr. Fernandez was asking about the calculation of the 95th percentile. Dr. Fernandez responded that he was, but because the sample size was 24, he did not believe that 1.645 is the correct value to use. Mr. Crowley responded that perhaps the value should be different because the sample size is lower than what is standard for using that figure. He agreed that this was a good point and could be valuable in terms of a recommendation. Dr. Fernandez added that the study assumes that the slope is equal in the five crops rather than testing this assumption. Dr. Philpott suggested that this point be reintroduced during the Board's discussion period.

Dr. Janice Chambers asked why the two sections of the OVS tube were analyzed separately. Mr. Crowley answered that this was discussed among the regulatory agencies in terms of concerns about breakthrough going through the full sampler.

Dr. Manautou noted the proportionality and independence between dermal exposure and AaiH, and mentioned that a relationship between dermal exposure and vehicle entrances and exits was found. He assumes that once the data from the open cab equipment are reviewed, it will address this issue. Mr. Crowley agreed that it would be useful.

Dr. Vanessa Northington Gamble commented that the language of the federal government should be used in EPA's reviews, and therefore not just "ethnicity" but "race and ethnicity" should be used.

Dr. Virginia Ashby Sharpe noted, on page 28 of EPA's report referencing the incidental exposures and failure of observer to intervene, that it states "until now neither EPA nor HSRB has focused on the application of protocol SOPs to the kind of situations described in this report." She questioned if this statement was referring to what type of activities or deviations should trigger an intervention. Ms. Sherman responded that the type of behavior that would cause the researcher to intervene was not a specific point of discussion. Occasionally, workers forget to put gloves on when exiting the cab. There could be value in this type of behavior from a science perspective in having those exposure points, but how far along a behavior that departs from SOPs should progress before being stopped by a researcher is unclear. Dr. Sharpe inquired, regarding the WPS advisor consult, given the terminology "treated surface," whether the worker

could put his/her hand directly into a tank containing pesticide and this would still be consistent with the WPS. Ms. Kathy Davis (OPP, EPA) replied that the WPS does not address that issue specifically, but if a worker was putting his/her hand in the tank to clean or conduct another activity in the handler description, PPE would be required.

Dr. Johnson asked how a glove could be removed without contaminating the other hand. Ms. Davis responded that there was a technique to safely perform this act.

Dr. Philpott invited AHETF representative Dr. Victor Cañez (AHETF Technical Chair, BASF Corporation) to respond to Board questions of clarification. Dr. Lebowitz questioned what the difference was between the California study and the other studies in terms of the WBD field fortification samples and targets of AaiH exceeding the upper limits. Dr. Cañez answered that for the field fortification sample, the AHETF conducted a thorough investigation to try to determine what the issues were; they were not limited just to California. Techniques have been revised, and sealed ampoules will be used in the future to get better results in the correct range. As far as the strata, that depended on what the grower was planning to do on the day of the study. Rather than cut the growers' day short, the data were simply collected. Dr. Lebowitz asked if the field fortification samples show residues or excessive residues, and whether the exposure data are adjusted accordingly. Dr. Cañez responded that this had been discussed with EPA, and if the values were systemically high, the AHETF likely would adjust them, but this would be done on a case-by-case basis. He was unsure whether the values were adjusted in this case.

Dr. Popendorf noted that specialized equipment used for low rate productions might fall into a lower stratum, and this was not part of the protocol. He asked if there was any information that would indicate that atypical equipment exists, specialized at the low end or otherwise, that was not assessed. Dr. Cañez replied that one or two experts asked about the equipment responded that it was not typical. In clarifying those responses, however, it was determined that there were many specialized sprayers and electrostatic sprayers that are meant to reduce exposure that were not captured in this protocol because the AHETF was not examining engineering controls.

Dr. Manautou asked if Dr. Cañez could explain why some samples are weathered and others are not prior to analysis. Dr. Cañez responded that it concerns when the sample could be contaminated or what residues could fall on the sample before the time it is actually collected, but for the hand washes and face/neck wipes, the samples are collected when they are taken, so those are not weathered. For the worker and WBDs, the residues could be present at minute one, but they will not be collected until the 4 hours are completed, so these samples are weathered, as are the samples in the OVS tubes. Dr. Manautou questioned whether the time of weathering was intended to mimic the length of time that a worker was in the field. Dr. Cañez replied that it was. The field fortification samples are prepared around the time the worker enters the field, and are collected when he/she comes in from the field.

Dr. Lebowitz asked for the upper range of the length of time that samples are stored before they are analyzed. Dr. Cañez answered that he would have to examine the analytical reports, but source stability data are available to indicate stability in all of the products. Dr. Lebowitz confirmed that the data in the reports are adjusted for the stability deviations. Dr. Cañez responded that he did not think that they were adjusted, but sufficient (80 to 100 %

recoveries) stability of the samples is demonstrated. In selecting surrogates, the AHETF examines stability and determines whether the material can be analyzed and the level of recovery.

Dr. Sharpe inquired about subject A4 in the Washington apple study who was observed not wearing gloves and the significance of the higher exposures related to the incidental exposures. Dr. Cañez responded that he did not know how the residues relate to the average, but the AHETF likely would determine the distribution of the residues, highlight some of the issues, and recommend that he wear gloves. Dr. Northington Gamble asked why the worker was not wearing gloves. Dr. Cañez assumed that it is his normal practice. The AHETF is trying to let subjects do their jobs in their normal manner. The subjects are provided with the product label when they start and researchers ensure that they read and understand it, but then they are allowed to conduct their normal practices. Dr. Popendorf noted that the protocol stated that the subjects were supposed to wear gloves when they were out of the cab, and asked if workers were told to follow the protocol. Dr. Cañez answered that part of the informed consent process is ensuring that the subjects understand the label requirements and what they are supposed to do.

Public Comments

Dr. Cañez noted that EPA's reviews had highlighted some issues that need to be changed, and as always the AHETF is willing to adapt and make this a process where deviations are reported.

Dr. Philpott invited additional public comments on the AHETF closed cab airblast applicator study; none were received. He noted, however, that one written comment was received in response to the *Federal Register* notice of the meeting. Ms. Barbara Sachau, writing under the alias Jean Public, raised some issues regarding EPA's failure to consider human exposures to lead through consuming hunted game. Dr. Philpott commented that this was not directly relevant to the issues before the Board, and probably was beyond the purview of EPA.

Charge Questions

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

1. Was the research reported in the AHETF completed monograph report and associated field study reports faithful to the design and objectives of the protocol, SOPs, and governing documents?
2. Has the Agency adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating exposure of those who apply conventional pesticides with closed cab airblast equipment?
3. Does available information support a determination that the studies were conducted in substantial compliance with subparts K and L of 40 CFR part 26?

Board Science Review

Dr. Philpott requested the Board members focus their discussion on the two scientific charge questions. Additional suggestions or recommendations can be submitted independently to the Agency or can be elaborated in the meeting report.

Dr. Lebowitz noted that Board members previously had discussed definitions of the terms in the charge questions. He believed that EPA's scientific reviews and analysis were well done. The studies were not totally faithful to the protocol and SOPs, however, and possible adjustments were not made. In some cases, estimating changes in exposures from hand contact could have been improved. He believed that the MEA was insufficient and must be examined. Once the MEA is more accurate, proportionality can be examined better. The statistical methods used were not necessarily ideal, and other probability distribution functions might be better. Data were anchored by using half the level of detection and level of quantitation, and this is inappropriate because it gives false regression results. Once further analyses are conducted, the data will be useful and the Agency will have characterized the estimated exposure adequately for those who apply conventional pesticides with closed cab airblast equipment. The data then will be useful for regulatory purposes.

Dr. Manautou stated that he was confused with the analysis showing dermal data are independent from exposure and the inhalation data are not. He requested better clarification on this point. Some of the deviations from the protocol are not that significant, so he concurs with Dr. Lebowitz on his assessment, but there may be a need to anchor the dermal versus inhalation data.

Dr. Fernandez noted that he had nothing further to add in terms of statistical analysis.

Dr. Johnson stated that the use of the term 80 percent power needs to be qualified every time it is used. The tables that involve the geometric standard deviation (GSD), intra-class correlation (ICC), geometric mean, arithmetic mean, and 95th percentile show CIs for those that may not be CIs, because a CI would imply that sampling is being conducted from a single population. In this case, sampling is being conducted from 25 different populations. The population varies for each cluster, and the AaiH is varied for each subject. The 95 percent may be the observed distribution. In addition, the log normal probability plots were surprising because the data fit so well. It would be useful if the symbols corresponding to each study site were added to the normal probability plots. He would like to see another normal probability plot that corresponds to the AaiH subgroup to determine if there is any pattern. The EPA presentation did not focus on the cab exits versus exposure, but the report went into more detail. Those analyses are interesting, but he cautioned that EPA must be careful about making any inferences from discoveries that the experiment was not designed to address. The governing document satisfies references for 1.4 for the CI width to the 80 percent power, but this should be referenced in the report. In the regression analyses, it might be useful to look at the residual plots, conduct the regression, regress the log exposure, then examine the residuals from the regression to determine if there are any outliers or worrisome trends.

Dr. Young noted that when she examined the residuals, stated outliers did not appear to be outliers. It may be a consequence of them being from 25 different populations that caused them to appear to be outliers in the original plot. Dr. Fernandez rightly had raised a question about the slope being the same for each study site. Dr. Young conducted an analysis on that and there is no evidence of difference. The variance component is estimated to be zero, but EPA should check this in future analyses. Regarding the figures in the tables mentioned by Dr. Johnson, one of the problems is that it is deliberative to get a spread of the AaiH, and as a consequence, that affects exposure. What does the average of all of those exposures mean, and does it represent anything of interest? This raises a concern about the stated first objective, and EPA should consider what the measures of geometric mean or arithmetic mean really indicate in this case, and is it what the sponsors are interested in? Her other broad comment was that, in general, the analysis should reflect the study design. She indicated that the analysis performed does reflect the study design, but other issues were included as well. It is fine to explore other issues, but it must be ensured that the appropriate model that reflects the design is used for the principal analysis.

Dr. Popendorf observed that on the air sample that was not used, it is correct that the sampling time is necessary to calculate concentration, but if the formula on page 10 of the report is used, the sampling time is not needed. The sample, then, still is valid as long as it ran for the entire application period, and such samples could be used in the future. He expressed concern that the hand contact was not discussed until the scientific review of the monographs (section 2.3). He had examined hand versus non-hand contact, and noted that the 10 subjects he found with hand contact showed a big difference, but one that was not statistically significant. EPA was correct to examine the number of cab exits and entrances, and might consider examining the correlation by running the residuals and a step-wise regression to see if the remainder correlates with the AaiH after taking out the effect of exits and entrances. Additionally, the protocol did not account for any assessment of what residue might be inside of the cab, and there may have been a fair amount. A wipe sample could have been taken or the history of vehicle use could have been reviewed. He ran a correlation with time inside the cab; it was significant and might correlate with residues present. This should be mentioned as a study limitation. When the open cab study is reviewed, the correlation may be present.

Dr. Chambers commented that in this case, the engineering control is so effective that the measured residues seen are from incidental exposures, and are not predictable. Therefore, the data sets will not be invalid if the proportionality is not seen.

Dr. Philpott stated that with respect to the science charge questions, the conclusion was that the study was not totally faithful to the protocol, SOPs, and governing document, but that there are adjustments that can be made, such as estimating changes in exposure due to hand contact that fell outside the protocol and other protocol deviations, that will give better estimates of exposures. The Agency characterized the limitations of the data very well. There were recommendations on some of the analyses; for the most part, the statisticians on the Board were pleased, but it was suggested that some terms be more clearly defined. If 80 percent power is used, what it is used for should be explicit. In addition, there were questions about the use of 95 percent CIs when sampling more than a single population. Although it was interesting that the additional exposures showed a correlation between dermal exposures and the incidental contact, it should be ensured that the analysis always reflects the principal points and objectives of the

study design. The focus on cab entrances and exits was interesting and some potential analyses would be useful. Even if proportionality does not hold for the dermal exposure, the data still would be useful for the purposes of the task force and the Agency, and may suggest that engineering controls are effective.

Board Ethics Review

Dr. Jerry Menikoff noted that available information supports a determination that the studies were conducted in substantial compliance with subparts K and L of 40 CFR part 26. He thanked EPA and Ms. Sherman for discussion of the detailed facts. The study is being conducted to answer a research question, and there are rules related to protection of subjects, but the point of the endeavor is not to protect the subjects; they should be protected consistent with the attempt to answer the research question. The overall design of the studies highly minimizes risks to subjects by creating a scenario in which, for the most part, subjects are doing what they normally do day to day. One major issue is the number of instances in which subjects did not wear gloves in a particular scenario; Ms. Sherman asked whether the goal of the research was supposed to be realistic and take into account what the subjects actually do while on the job. Subjects were informed that PPE should be worn, and they reviewed the consent form; it appears that workers do not always wear their gloves. Six out of 24 subjects removed their gloves in at least one instance. The protocol could have been written in a way that would not have made this a deviation, but the removal of gloves is not a significant ethical issue. He noted that these compounds were chosen because they were relatively low risk. The protocol does currently seem to state that each time a subject removes PPE, he/she should be warned. This is an issue that should be clarified in the future.

Dr. Sharpe agreed that the study was conducted in substantial compliance with subparts K and L of 40 CFR part 26. Her impression on the issue of the workers not wearing their gloves is that it was just sloppiness. She is unsure whether or not it was sloppy on the part of the observer because the observer understood this to be strictly an observational study, which it was not. This issue does not, however, rise to the level of risk. Understanding the research as observational could be considered self-serving, because it provides additional data that the researchers were not seeking explicitly. It would be interesting to discuss whether this series of incidents should result in an SOP with additional guidance recommended to observers when they witness such behaviors. She is troubled if there are observers who are not trained sufficiently or do not have sufficient judgment to maintain the protocol requirements. That may in some cases, although not in this case, have implications on subject safety.

Dr. Northington Gamble suggested that some additional information could have been obtained by the observer as to why the subject was not wearing gloves, and she found it troubling that the observer did nothing.

Dr. Philpott stated that the Board must decide whether the HSRB will be making the recommendation that the sponsor and the Agency consider drafting an SOP about creating a threshold for when intervention should occur. That is a difficult question, but gets to the point about variation among the observers and their understanding of the research goals. Without the SOP, variability could be introduced, and that could influence the study results.

Dr. Popendorf reminded members that during the past year a protocol came to the Board in which clarification was requested on the same point: if a subject violated the protocol, how severe would the violation have to be before the person was not used as a subject?

Dr. Philpott did not know whether that issue had been resolved. He believed a suggestion was made to the Agency and sponsors that they determine some objective criteria on when subjects should be excluded from participation because of their behavior. In this case, the Board is asking whether criteria are needed for when observers should intervene to correct potentially dangerous behaviors in the subjects, recognizing that some of these behaviors represent normal activity, which is exactly the data that the Agency and sponsors hope to collect.

Dr. Menikoff agreed that this is a relevant issue and suggested that it may be useful for sponsors to collect data from the person who is not wearing gloves; the protocol should not over-instruct subjects to a point of getting unrealistic behavior. There are other design elements in the study that correct for most of the egregious behavior. Subjects are well-trained and have been doing the studied work for 3 or more years. It may not be the Board's place to tell the sponsor how to resolve this other than stating that it is a protocol issue. Scrupulous protocol adherence would have been for observers to warn subjects to put on PPE, but this may produce data largely deviant from what applies in the field.

Dr. Philpott stated that the Board's conclusion is that yes, studies were conducted in substantial compliance with subparts K and L of 40 CFR part 26, and that acknowledging the protocol deviations, the HSRB agrees with EPA's assessment that they did not substantially increase risk to participants or compromise their safety. More importantly, the Agency and sponsors must consider whether they want absolute adherence to the current SOP that states that if there is deviation from the label, there will be an intervention, or whether they want to modify the SOP to reflect more accurately day-to-day practices on the part of the pesticide handlers. The HSRB is not making a recommendation either way, except to say that this point needs to be considered. There is consensus that the Board carefully would consider changes to the SOP to reflect actual conditions if there were potential risks, but it is not making any specific recommendations at this point.

Session 2: AHETF Scenario Design and Associated Protocol Describing Proposed Research to Monitor Exposure of Workers Who Mix and Load Pesticides Formulated as Wettable Powders

Background

Ms. Sherman informed the Board that this protocol was similar to one reviewed in October 2010 for wettable powder (WP) in water-soluble packaging. This protocol is similar in that: design objectives, sample size, and rationale are similar to several previous AHETF scenarios reviewed; there is a 5x5 cluster configuration; and protocol procedures related to ethical conduct are similar. It differs from other AHETF protocols in that: one of the five clusters, a preexisting pre-rule study using diazinon as the surrogate already is completed; it monitors mixers and loaders; and it uses three new surrogates, dimethyl tetrachloroterephthalate

(DCPA), sulfur, and thiophanate-methyl (copper was originally a surrogate, but was withdrawn). The protocol submission contained all elements of documentation required by 40 CFR §26.1125 in the form of one main submission document and a supplement. This protocol was submitted to the Agency in early October 2010 before the previous HSRB meeting, so instead of rewriting the protocol, the AHETF included the supplement to reflect the changes suggested by the Board in October 2010. EPA believes that this proposal is ready for HSRB review.

EPA Science Assessment

Mr. Jeffrey Evans (OPP, EPA) agreed that the protocol was very similar to the one on WPs in water-soluble packaging. WPs are the most basic simple formula available, and are widely used in agriculture. The scenario uses a single layer of clothing, long pants, long-sleeved shirt, shoes, and socks, and the only required PPE is chemical-resistant gloves. Dust masks and protective eyewear can be worn if subjects choose. There are three sub-scenarios that are used to account for the fact that there are differences in the way that the material is added to the tank. They include mixing of WPs: directly into the tank used for the pesticide application; into a large "pre-mix" tank at the same concentration to be applied to the crop by a number of application types; and into a tank or bucket as a concentrated slurry that must be further diluted and transferred to the final application tank.

There will be five clusters containing five monitoring units (MUs) each. The existing study (AHE39), completed before the enactment of EPA's rule, involved the mixing and loading of a WP formulation of diazinon. This study included WBD and all body parts were accounted for in terms of measurement. Potential drawbacks, however, include lack of the Board's input in terms of the statistical design, the narrow range of AaiH mixed and loaded (59 to 138 lbs ai) and the fact that the study consisted of only one sub-scenario (concentrate in pre-mix tank or bucket). That study will be added to four new clusters with five MUs each. EPA insists that all three sub-scenarios be performed at each new cluster, and notes that respirators may be required with certain products.

EPA hoped that copper would have been included among the surrogates, but the interferences of copper on the WBDs from pre-washing were too significant. The three surrogates that will be included in the new clusters are: DCPA (dacthal), an herbicide with low dermal toxicity (but requiring a respirator for mixing and loading WPs because of inhalation toxicity) used on many vegetable crops; sulfur, a fungicide and insecticide having high application rates and low acute toxicity; and thiophanate-methyl, a widely used fungicide, but with AaiH in this study limited to 100 lbs because of exposure estimates. It is suggested that thiophanate-methyl be used for the lower strata.

The proposed AaiH strata include the following requirements: all monitoring durations will be at least 4 hours; each subject will mix and load at least three tanks of spray mixture; and five strata of AaiH will be included in each cluster. The proposed monitoring areas ensure diversification of equipment types by including different growing regions of the country, different crops, and different climates. Given the limitations of AHE39, the researchers must ensure that each of the three sub-scenarios be monitored at least once within each cluster, and that participants apply AaiH from each of the five strata per cluster.

EPA Ethics Assessment

Ms. Sherman presented EPA's ethics assessment. She began by noting that the current data on this exposure scenario do not meet contemporary standards, so newer and better data that would be generated through this research are needed to support EPA risk assessments. The research will be combined with existing data and used to estimate dermal and inhalation exposure for a wide range of pesticides. The subjects in the study will be recruited from growers and commercial pesticide application companies; once eligible growers are identified, the study director will seek permission to approach the employees to recruit subjects. Recruitment will take place with the use of a flyer posted in the workplace, or the study director will hold a meeting with interested employees to discuss the study and answer questions. Employers are not to attend recruitment meetings. Subjects who have experience within the past year performing mixing and loading with a WP product and who meet other eligibility criteria are recruited. The protocols and SOPs provide procedures to protect employees from potential employer coercion. Employers are asked to sign a non-coercion statement affirming that they will not coerce or influence their workers in their decision whether to participate, and also must agree that they will provide alternate work on study days to workers who choose not to participate. They also agree that the decision to participate will have no impact on the employees' future employment.

The consent process consists of a private meeting between the study director and subject. There are equivalent processes in the protocol and SOPs for Spanish and English speakers relying on bilingual investigators to perform the meetings in Spanish. The consent form contains all of the elements required by 40 CFR §26.1116, and Ms. Sherman concluded that the organization and presentation of risk information in the consent forms are acceptable.

In terms of respect for subjects, the payments proposed are reasonable, subjects are free to withdraw from the study at any time for any reason, individual results will be provided to subjects upon request, medical care for research-related injuries will be provided at no cost to the subjects, and there are procedures to protect subject privacy related to participation in pregnancy testing. The four overarching considerations in evaluating the recruiting consent process are met: subject selection is equitable; subjects are given the opportunity to make a fully informed choice about participation; participation is fully voluntary; and there is respect for subjects.

In response to comments that the Board made in October 2010, risk of exposure to surrogates has been added back into the discussion of risk in the protocol and ICFs. Ms. Sherman concluded that the procedures in place minimize the risk related to participation in the study to the greatest extent possible. To minimize the risk of exposure to the surrogates, the researchers are using materials that have been widely tested and are proposing to have the subjects use them at levels associated with safe exposures. The participants will be selected from workers with experience performing the work being monitored, and they are therefore less likely to misuse the chemicals. Before the study begins, the participants will be reminded about safe practices and procedures and to wear appropriate PPE.

In terms of heat-related illness, exclusion and eligibility criteria only allow subjects who are reported to be in good health. Subjects are closely observed during the monitoring period,

and research staff are trained to recognize signs and symptoms of heat illness. There will be medical staff onsite and a stopping rule stating that the exposure monitoring will be stopped if the heat index exceeds 105 degrees Fahrenheit. A question was raised in October 2010 about who would make the determination that a subject would be considered too ill to make a rational decision about declining medical care; the medical professional onsite would make that determination.

The risk of scripting field activities is expected to be small because the workers are not being asked to use equipment that they are unfamiliar with but may result in them applying more pesticide or working longer or shorter than they would have otherwise, and the extended work period could raise the risk of related illness. The psychological risk is minimized by providing for private handling of the pregnancy testing results and having a same-sex researcher present during dressing in the dosimeters. Risk of skin irritation from exposure to surfactants (soap for hand, face, and neck wash) is expected to be small.

EPA concluded that the protocol provides a favorable risk-benefit balance. Subjects will be monitored while they perform their normal work so risks will not be much greater than what they would face normally. Although there are no direct benefits to the subjects, the risks have been properly minimized and therefore will be reasonable in light of the potential societal benefits of more accurate risk assessments from the generated data.

The AHETF has been responsive to EPA and HSRB comments in its supplement to the protocol. The task force has identified exposure to surrogate chemicals as a potential risk of study participation. When instructed to ask potential participants about what PPE they normally wear in a non-directive manner, the AHETF noted that this was its normal practice. EPA suggested that the AHETF revise its SOP on this process to acknowledge this concern. Because of the Board's recommendation, the AHETF's protocol now states that hand washes will be conducted before eating or smoking. EPA raised the issue that the AHETF should clarify whether hand washes will be required before water breaks. Requiring hand washes before every water break could result in additional exposures to the surfactants, however, and therefore may make subjects hesitant to take a water break. Conversely, not requiring the hand washes may increase hand-to-mouth exposure and may confound the results if some of the subjects are conducting hand washes but others are not. The next Board comment suggested that the AHETF address how individual exposure information will be released to subjects who request it, and asked that a check box be included on the ICF. In addition, the Board recommended that the task force explain how exposure information will be provided to subjects who might not speak English and/or are illiterate. This issue has not yet been addressed. There is an HSRB working group on the topic that will provide advice when available, so Ms. Sherman recommended that the AHETF incorporate that advice and the process into an SOP. The task force will test the representativeness of the sample and the accuracy of Spanish translations; EPA suggested that these actions be added to the SOPs. ICFs now explain that the researchers provide the pregnancy tests, and explain when the test will occur. Additionally, it has been clarified that individuals who are exempt or performing work not covered by the WPS are eligible to become subjects without WPS training.

IIRB reviewed and approved the protocol, and its roster and Human Research Protection Program plan are on file with EPA and have been provided to the HSRB. The protocol is a proposal 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. The primary ethical standards applicable to the conduct of this research are 40 CFR 26, subparts K and L and the Federal Insecticide, Fungicide, and Rodenticide Act 12(a)(2)(P). EPA concluded that the protocol meets the applicable ethical requirements of 40 CFR 26, subparts K and L, and did not note any deficiencies.

Board Questions of Clarification

Dr. Popendorf sought justification for the upper range in the protocol, and asked if achieving it was feasible. Mr. Evans responded that EPA believed that it was. The AHETF is fully aware of the values EPA uses in its assessments. Given the application rates of sulfur, it is quite feasible for workers to get into the high range (604 to 2,000 lbs ai handled). Sulfur is applied at the rate of approximately 8 lbs per acre. Dr. Popendorf commented that he had not noticed the language in the protocol stating that each new cluster will have all three sub-scenarios. Mr. Evans replied that he remembered reading this, but that EPA was insisting on this point. Dr. Popendorf asked if there was a reason that all new clusters will contain all five strata. If that is done, the results will be a 4-4-9-4-4 distribution. Within Appendix C, the modeling came up with a factor of 3. They looked at clusters, and the distribution of MUs in clusters, but Dr. Popendorf did not know if strata were included. If they are, would the resulting 4-4-9-4-4 distribution violate the broad criteria that structured the factor of three? Mr. Evans answered that it was impossible for EPA to know what will happen, but diversifying the strata is key for the secondary objective. If 20 MUs are fully diversified, the limitations of the five existing MUs would be minimized. Dr. Popendorf suggested that unless there was some rationale for repeating the middle strata, the researchers should use the five from the existing study and distribute the next 20 MUs throughout the other four strata. Mr. Evans asked if this would affect ICC analysis. Dr. Philpott suggested that this be addressed during the Board's discussion period, and noted that two questions posed could be better asked of the AHETF.

Dr. Sharpe noted that one of the slides in EPA's presentation stated that respirators may be required for certain products, and asked if this would be clarified in terms of which chemicals would require a respirator. All of the photographs in EPA's presentation showed workers using respirators. Mr. Evans answered that many times, the requirement for a respirator is based on the acute toxicity of the unused product. There are many products of this type, so it is likely that some are based on the concentration.

Dr. Sidney Green pointed out that on page 19 of the protocol, in text discussing overhead cost associated with obtaining efficient configuration, the last two sentences in the paragraph carried over from page 18 seem to be incorrect. Should it state "monitoring areas less cost-effective"? Mr. Evans agreed that the text was confusing. Dr. Green also questioned if in the table on page 31, the entries on sulfur and total ai usage on strawberries and cherries were incorrect, because all other entries were in descending order of amount. Mr. Evans admitted that this would be answered better by the AHETF. Dr. Green noted that the last confusing instance was on page 273 in the SOP. On the third line of paragraph B, the study mentions "drug and

device" procedures. There are no drugs and no devices in this protocol. This procedure may have come from the U.S. Food and Drug Administration's (FDA) guidelines. He suggested that "drug" and "device" are inappropriate in this instance, and "chemicals" should replace them. Mr. Evans agreed. Dr. Philpott suggested that this was a recommendation for the sponsor.

Dr. Manautou asked if there was any relevance of the crop type to the proposed protocol. Mr. Evans responded there was not, but various crops allowed an opportunity to find participants who use one of the surrogates and the ability to find at least five different equipment types.

Dr. Popendorf questioned why subjects may be asked to work longer than they normally would during the study. Ms. Sherman responded that this point was meant in relation to the concept of scripting their work for the day of the study; the time of monitoring and AaiH could be slightly more than under normal circumstances. Dr. Philpott added that the time required to put on the WBD may add time to the workers' day as well.

Dr. Northington Gamble noted the protocol's mention of the use of witnesses for people of low literacy; it states on page 292 that the witness would be identified by the study director. It then lists the protocol that had been discussed previously by the HSRB on how the witness would be identified, which is in conflict with the previous statement. Ms. Sherman replied that the statement "identified by the study director" may have been carried over from older protocols. She will examine the issue to see if the procedure is included in the SOP. The intention is that the worker can identify a witness of his/her choosing. Dr. Philpott stated that this may be a recommendation.

Dr. Philpott invited Dr. Cañez to respond to Board questions on behalf of the AHETF. Dr. Philpott asked whether having an upper limit of 1 ton of AaiH was feasible. Dr. Cañez answered that he could not name products that could be used at those rates, but when studies are designed, members are asked what products fall into specific categories. The AHETF will then examine the product labels and determine the ranges of AaiH needed. There may not be many that reach the higher limit in this protocol, but some may be in the higher strata. Dr. Popendorf asked if the products that might be used at the high level or information on how the level was determined were listed in the protocol. Dr. Cañez noted that it should be listed in the scenario design document.

Dr. Philpott asked whether the modeling accounted for the fact that the pre-rule study (AHE39) was biased toward the middle strata, and whether that may affect the 5x5 cluster design. Dr. Cañez answered that for the cluster design, the AHETF depends on Dr. Larry Holden (AHETF Statistician, Sielken & Associates) to generate those monitoring areas and clusters taking into consideration the existing data. The study design document should contain an analysis of how the existing data can fit with the new protocol.

Dr. Lebowitz asked which chemical surrogates will be used in which clusters because mixing scenarios differ. Dr. Cañez responded that it was known what crops the products were used in, and the AHETF will call many growers in those areas to achieve the diversification needed. It will be a challenging task. Some products that are used at very low use rates must be placed in the smaller strata, and those may be mixed directly into the tank. Some of the products

that are used in the upper strata at higher use rates, such as sulfur, are more likely to be added to pre-mix tanks.

Dr. Northington Gamble noted a discussion at the previous HSRB meeting on the selection of subjects who are in good health. In the protocol, it stated that people who say they are in good health are accepted, but there are no health criteria stated. Are there certain health conditions that would exclude someone from participating in the study? Dr. Cañez responded that the AHETF did not want to get into the practice of having criteria in the process, so subjects are allowed to self-report and must indicate that they have done the type of work being studied within the past year. Dr. Philpott commented that at the previous HSRB meeting, there was a concern about a participant who reported that he was in fair health, but was enrolled in a study anyway after the investigator met with him and made an assessment. The HSRB recommended that there be clear objective criteria as to what constituted good health. It may be something such as having engaged in the physical work within the past month, but the AHETF may want to consider some objective criteria. Dr. Northington Gamble added that if someone states that they are in fair health, they should not be included in the study. Dr. Cañez replied that in this protocol, there was not an option for "fair health": the subject would identify as in good health or not in good health. Ms. Sherman added that there is an SOP (11.2.1) on worker health status that states that the workers must be in good health.

Dr. Philpott asked if the requirement of the respirators as PPE is chemical-specific or if all individuals would be required to wear respirators. Dr. Cañez responded that the AHETF was following the product label requirements. Dr. Sharpe asked if this would be reflected in the ICF and protocol, because she did not believe that it currently is included. Dr. Cañez answered that the informed consent process will include the label for the product that will be used, and the label requirements would be reviewed with the study candidate.

Dr. Sharpe mentioned a new line in the paragraph about pregnancy testing stating that more than one pregnancy test may be required and asked for the reasoning behind that and whether it would be explained further in the ICF. Dr. Cañez stated that he was unaware of the line. Ms. Sherman added that she had seen the line and had a question about it as well. Dr. Philpott added that the HSRB had seen a study at a prior Board meeting in which there were multiple activities on multiple days; the way the regulation was written erred on the side of caution, and perhaps that was the source of the statement. Dr. Cañez added that it may have stemmed from the potential delay from the informed consent process to the actual monitoring, but that he would investigate. Dr. Sharpe added that it would be useful to explain the reasoning in the ICF if more than one test is required.

Dr. Philpott noted Dr. Green's questions regarding an error on page 19 regarding cost-effectiveness, and on the distribution of crops in a table on page 31. Dr. Cañez replied that it is more cost-effective to get more MUs in one place, but he would investigate the potential errors and get back to EPA.

Dr. Johnson commented that section 4.5.1, pages 23-24 of the protocol, discusses the GSD and the existing study ICC and mentions a chi square distribution. He asked for either a greater explanation of the chi square, or that it be removed from the protocol. Dr. Young added

that the GSD to the square root of 1-ICC was confusing, and a reference would be useful. Dr. Philpott noted that these were points to be addressed during the Board's discussion period.

Public Comments

Dr. Philpott called for public comments on the proposed AHETF scenario and field study (AHE80); no public comments were presented.

Charge Questions

Ms. Sherman read the charge questions into the record:

If the proposed AHETF scenario and field study (AHE80) is revised as suggested in EPA's reviews and is performed as described:

1. Is the research likely to generate scientifically reliable data, useful for assessing the exposure of workers who perform open mixing/loading of pesticide end use products formulated as wettable powders?
2. Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

Board Science Review

Dr. Popendorf raised three points related to the strata. The upper 2,000 lb limit likely is reasonable when mentioning sulfur, but he could not find the reference to how that limit was generated in the protocol. The second point related to the lower estimate, and whether the equipment used is typical. Perhaps some of the limitations and what is not being assessed could be discussed. Thirdly, the guidance on pages 27-30 discusses addressing the issue of clusters, but did not address the use of strata. He noted that the way the next 20 MUs are distributed among the five strata is a concern; if they are uniformly distributed, a 4-4-9-4-4 distribution will be created, and this may violate the criteria in Appendix C. Additionally, it may not be good science, because too many data may be clustered in the middle.

Dr. Green noted no concerns regarding the science associated with the scenario; his only concerns were the three issues to be clarified in the protocol and the SOPs. His response is yes, the protocol would provide scientifically reliable data.

Dr. Young stated that regarding Dr. Popendorf's concern about the distribution over the strata, some simulations may have to be conducted. She believed, however, that he was right, and that the data will be too clustered in the center to give appropriate power. She reiterated her point about the GSD calculation, and also expressed concern about the chi square calculation; they need to be defined better. She added that if there is not an association between exposure and AaiH, treating it as a log normal and determining a mean is reasonable. If there is an association, however, taking an average is forcing more diversity than normally would be reflected in a sample, which may be useful. Dr. Young also stated that the sample should not be treated as random. Overall she felt the explanations were well-documented throughout the protocol.

Dr. Johnson agreed that Dr. Young's ideas about simulation could be useful for future studies. Additionally, the existing study had all mixtures as slurries, and this may raise the same issues as the distributions of MUs. Dr. Popendorf agreed, and asked that EPA ensure that this issue is in the final protocol; each cluster should have all types of mixing and loading performed. He also agreed that simulations would be useful, but suggested that they be run with five in each cluster, adding all the new MUs to the two lower and two upper strata. Because if the middle strata is doubled, power will be lost. Dr. Young agreed, and added that she questioned what it meant to average all of the different kinds of mixes and AaiH. Dr. Popendorf agreed that this was an unknown. Dr. Lebowitz also agreed, and added that the chemical used for each mixture might be important. With the slurry in the middle strata, adding data above and below will provide a good regression line. That may be worrisome based on the design, and a simulation may help to predict what might happen. Mr. Evans added that he had held several e-mail conversations with Dr. Holden, who stated that the AaiH levels tend to be forgiving to a point. The secondary benchmark often can be met if only some of the clusters span the practical range of AaiH. The separation into exact strata is less important than the ability to span the AaiH range. Mr. Evans found this compelling in terms of conducting the next four clusters as if there were five. Dr. Johnson noted that Dr. Holden seemed to agree with him and Dr. Young.

Dr. Philpott stated that the Board's general consensus regarding whether the research is likely to generate scientifically reliable data useful for assessing the exposure to workers under this scenario is yes, but with limitations. He noted that Dr. Popendorf had raised some concerns about how the range of the strata was generated, which was not clear to him in reading the protocol, and that each of the remaining four clusters must have all three of the sub-scenarios included. There seemed to be broad agreement that given the fact that the previous AHE39 study was biased towards the middle strata and only was a slurry scenario, it may be useful to conduct some simulations to determine whether the desired power can be achieved by just moving forward with the remaining four clusters across all five strata with all three sub-scenarios represented, or whether the remaining MUs should be distributed differently. The question was raised as to whether this distribution may affect the scientific validity of both objectives but particularly objective number two. There were concerns about how the GSD and the ICC calculations were conducted in Section 4.5.1 of the protocol, and a request for more explanation and some references for the calculations was made. It was stated that using a log normal is correct if there appears to be no association between exposure and the AaiH, but if there is an association, that raises questions about the appropriateness of treating a forced diversity sample as though it were random. He added that Dr. Green noted that there were some potential errors in the protocol, particularly with respect to cost effectiveness on page 19, the crop distribution table on page 31, and concerns about the language used for adverse event reporting that seems to be language from the FDA.

Dr. Popendorf asked that the rationale for the 2,000 lb upper limit in the protocol be pointed out, and that if it was found, that the final meeting report reflect that he had missed it. Dr. Philpott explained that the Board's recommendations are not finalized until the final meeting report is released. The draft report will be discussed during a public teleconference. Therefore, if Dr. Cañez or Mr. Evans can identify the area concerned in the protocol and notify him and Mr.

Downing via e-mail, the response will be forwarded to Dr. Popendorf and that recommendation can be removed.

Board Ethics Review

Dr. Northington Gamble stated that the research is likely to meet the applicable requirements of 40 CFR part 26, subparts K and L if some issues are resolved. One point is to ensure that people are fully informed of their choice to participate. To have the best practices in terms of informed consent, the discussion must consider more than ethics, and in this case must consider literacy, which often is conflated with reading. The following definition of health literacy is from the Department of Health and Human Services' national action plan on health literacy: "the degree to which an individual has the capacity to obtain, communicate, process, and understand health information and services in order to make appropriate health decisions." Literacy is not just about reading, but also about comprehension. The words "illiterate" and "non-reader" should not be used; instead use terms such as "low literacy" or "limited literacy." These should be changed in the protocol, as should statements such as "the reading level of the English speakers was appropriate." The actual reading level should be defined in both English and Spanish, and Spanish used should be defined by dialect.

Dr. Northington Gamble added that the change to the language about refusing medical treatment must be revised. The use of the term "rational decision" is a concern. EPA approached some other points of revision well, such as the language surrounding the PPE that subjects normally wear while working, and the fact that hand washing before water breaks needs to be clarified.

Dr. Sharpe agreed that more modifications are needed so that the protocol and ICF will be in compliance with the regulation. She asked Ms. Sherman about the identification of the return of research results as an indirect benefit of the study to participants in EPA's review. The study states that there are no benefits to the subjects, and Dr. Sharpe agreed, and believes that EPA should remove the statement from its report. Her other point involves the protocol identifying the study as greater than minimal risk on page 106 and again in the supplement. If the surrogate chemicals are to be added as one of the possible risks, the addition must be made in a number of different places in the protocol and in the SOP. The protocol now states that the study is of greater than minimal risk in particular because of heat-related illness, which is too narrow because the addition of the surrogates as a potential risk needs to be reflected in the protocol, the SOP 11.J.2, and the informed consent checklist. The governing document states that the AHETF does not consider the risk of toxicity for pesticide handling to be strictly due to study participation, but it is if the study includes surrogates.

Dr. Chambers stated that her understanding was that a pesticide would be applied to that field with or without the study, and it could be the same one or a different one. These workers would be doing their normal tasks, perhaps with this chemical or perhaps with another one. They may or may not be doing something different in the study than they would otherwise.

Dr. Philpott noted that a risk of study participation is that participants may be using a surrogate compound that they normally would not use, and handling different amounts or using

equipment that they normally would not use. Dr. Sharpe has stated that the AHETF must go back through all of the SOPs and documents to ensure that exposure to the surrogate pesticide is classified as a risk. Dr. Sharpe added that other areas may need to be modified because of the addition of that potential risk.

Dr. Popendorf commented that there are several uses of the word "surrogate." In some cases a chemical other than the pesticide in question is a surrogate. The data that result from this use are considered surrogate data for any other pesticide. Dr. Sharpe clarified that she was using the word in the first way Dr. Popendorf mentioned. Dr. Popendorf added that in this case, the participation of the subject is predicated on the fact that they are going to apply the pesticide to be studied.

Dr. Philpott stated that the recommendation about adding the risk of surrogate chemicals to the protocol was made at the last Board meeting for the previous protocol. The recommendation can be made for this protocol as well. Dr. Sharpe noted that Dr. Popendorf had explained that it may not be applicable in this study.

Mr. Jordan confirmed that the task force drafted the protocol and submitted it to EPA before the October 2010 HSRB meeting, and that is why the protocol did not include any reference to surrogate chemicals and the risks associated in either the informed consent materials or the assessment of risks and benefits. The task force submitted a supplement to the protocol, which contained language about how they would amend the informed consent documents to address that consideration. EPA is considering the point that Dr. Menikoff raised in October 2010 and that the Board accepted and endorsed in its meeting report; by asking participants to use pesticides that they might normally be using but by constraining that use through the scripting process, the exposure profile might differ compared to what those participants would have experienced otherwise, which might amount to a difference in risk. The pesticide use that would go forward under the protocols would be consistent with the product labeling and would have an acceptable level of risk.

Dr. Popendorf pointed out that Mr. Jordan never used the term "surrogate," so what he said would apply to any study that involved exposure to pesticides. Mr. Jordan noted that in EPA's parlance, the word surrogate is used to mean that the chemical tested will be used to represent other pesticide chemicals.

Dr. Philpott added that "surrogate" is being used in multiple ways across multiple studies, and the Board members must be careful as to how they use it.

Dr. Chambers postulated that an insecticide is needed on a particular field of the grower that is participating. He has a choice of several that are approved for that purpose, but there is only one surrogate like carbaryl, in this case, that is stable and analyzable enough to serve as the surrogate. So carbaryl is used but others could have been used as well. She thought that this was the reasoning for the use of the term "surrogate." Mr. Jordan responded that she was correct. The recruitment process asks growers what pesticides they use, and the investigators do not steer growers toward use of a chemical but rather narrow the pool of potential growers down by finding out what they use.

Dr. Lux noted that the regulatory distinction between an intentional exposure study and an observational study is critical. If a study meets the regulatory definition of an intentional exposure study for any reason, including scripting, then the exposure becomes a risk of the research. In this study and in most of these studies, that research risk is very minor and is not the biggest risk of concern. By contrast, an observational study under the regulatory definition examines exposures that occur naturally without being in any way influenced by the research and, therefore, cannot be considered a risk of the research.

Dr. Northington Gamble commented that EPA's review states that "in this study, risks to subjects are classified as greater than minimal, primarily since agricultural work is considered a high-risk occupation where the likelihood of harm or discomfort is greater than what is encountered in ordinary daily life." Therefore, all these studies could be said to have a greater than minimal risk. Dr. Lux explained that he used the term minor because minimal risk has a regulatory meaning that is highly contested in the bioethics community.

Dr. Sharpe confirmed that the outcome of this conversation may be a recommendation to go back to EPA's report on page 15, and possibly the protocol on page 106, to examine if this minimal risk issue is accurately characterized consistent with what has been added to the protocol.

Dr. Philpott stated that this was a recommendation both to the sponsors to ensure that the risk of exposure to the pesticide is accurately reflected everywhere in the protocol and in the informed consent documents, and also a recommendation to the Agency to examine its review and how risks were characterized, particularly in terms of minimal or greater than minimal.

Dr. Sharpe added that on page 288 and in the supplement, there is an issue with how to phrase the paragraph stating that the medical professional onsite will provide care and decide whether subjects are too sick to make a rational decision about refusing medical treatment. She seconded Dr. Northington Gamble's recommendation about the need for some criteria that are consistent with the literature about decision-making capacity. In terms of the word "rational," the recommendation may be to delete it. The medical professional needs to determine, based on medical criteria, that the person is too sick to make a decision.

Dr. Lebowitz agreed that medical criteria should be used because he assumed that medical personnel will use that rather than whether the person is rational enough. As a point of clarification, agricultural work presents a greater than minimal risk. Pesticide-specific usage causes a minor risk increase. The terminology has to distinguish between those two aspects. The terminology, however, is appropriate.

Dr. Philpott noted that the following points should be included in the recommendations: the sponsor should define "good health" as a criterion for study inclusion; explain why more than one pregnancy test may be required; and clarify in the SOPs that witnesses are to be chosen by subjects with low literacy versus study directors. The consensus of the Board is that the response to the question as to whether or not the research is likely to meet the applicable requirements for 40 CFR part 26, subparts K and L is yes if the protocol addresses the concerns identified by Ms.

Sherman in her ethics review and points raised by the Board members, including Dr. Northington Gamble's input to ensure that literacy is not conflated with reading and that use of terms like "illiterate" or "non-reading" can be considered offensive. Dr. Northington Gamble added that when asked if they are non-readers, subjects might say that they can read because of the stigma attached to being a non-reader. Dr. Philpott commented that sponsors also should be specific about what "appropriate reading level" means, and ensure the dialect of Spanish used represents the dialect of the study population. In addition, "rational" should be deleted from the concept that a medical professional may determine that a subject lacks capacity to make a "rational" decision, and instead clear criteria for assessing capacity should be used. Also, investigators should ensure that discussions about PPE do not sway individuals to use different levels of PPE than they normally would to participate in the study; remove the return of results as a potential benefit as described currently until the workgroup makes recommendations about how those results should be returned and the ethical basis for providing that information to study participants; and ensure that exposure to the pesticide as a potential risk of study participation is added back into the protocol and SOPs.

Dr. Young stated that Mr. Sarkar had been helpful in explaining the derivation in question, but that has raised some other concerns that will be addressed in the final Board report. Dr. Johnson added that the section in question could be removed, and Dr. Philpott noted that may be the Board's recommendation, but the Agency should wait until the final report containing the HSRB's final recommendations is issued.

Dr. Philpott thanked Board members, Agency staff, and public participants for their participation in the meeting and flexibility in completing the study reviews quickly.

Preview of Upcoming Meetings

Mr. Downing announced that the next HSRB meeting would be held during the week of April 11-15, 2011, at a hotel in Crystal City, Virginia. The notice of the exact dates, times, and location will be published in the *Federal Register* and posted on the HSRB Web site.

Adjournment

Mr. Downing adjourned the meeting at 3:17 p.m.

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.S. Bioethics — Term: 3/27/2006-10/31/2011
Director, Research Ethics
The Bioethics Program
Union Graduate College-Mt. Sinai School of Medicine
Schenectady, NY

Vice Chair

*Janice Chambers, Ph.D., D.A.B.T. — Term: 3/27/2006-10/31/2011
William L. Giles Distinguished Professor
Director, Center for Environmental Health Sciences
College of Veterinary Medicine
Mississippi State University
Mississippi State, MS

Members

*George C.J. Fernandez, Ph.D. — Term: 5/1/2010-8/31/2013
Director, Center for Research Design and Analysis
University of Nevada – Reno
Reno, 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

*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) & 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
Department of Health and Human Services
Rockville, MD

*^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
Washington, DC

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

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
Department of Statistics
Institute of Food and Agricultural Sciences
University of Florida
Gainesville, FL

*Special Government Employee (SGE)
^Not in attendance on January 26, 2011

Attachment B

Federal Register Notice Announcing Meeting

[Federal Register Volume 76, Number 8 (Wednesday, January 12, 2011)]
[Notices]
[Pages 2107-2109]
From the Federal Register Online via the Government Printing Office [www.gpo.gov]
[FR Doc No: 2011-625]

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ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-ORD-2011-0970; FRL-9252-3]

Human Studies Review Board; Notice of Public Meeting

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The U.S. Environmental Protection Agency (EPA or Agency) 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, 2011, from approximately 8:30 a.m. to approximately 5 p.m. Eastern Time. The meeting will be held at the Environmental Protection Agency, Conference Center--Lobby Level, One Potomac Yard (South Bldg.), 2777 S. Crystal Drive, Arlington, VA 22202. 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 10 business days prior to the meeting to allow EPA adequate time to process your request.

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.

ADDRESSES: Submit your written comments, identified by Docket ID No. EPA-HQ-ORD-2011-0970, 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-2011-0970. 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 disk or CD-ROM 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:

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). Since other 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. EST, 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). EPA's position paper(s), charge/questions to the HSRB, and the meeting agenda will be available by mid January 2011. In addition, the Agency may provide additional background documents as the materials become available. You may obtain electronic copies of these documents, and certain other related documents that might be available electronically, from the regulations.gov Web site and the EPA HSRB Web site at http://www.epa.gov/osa/hsrb/. For questions on document availability, or if you do not have access to the Internet, consult either Jim Downing or Lu-Ann Kleibacker listed under **FOR FURTHER INFORMATION CONTACT**.

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

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

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

D. How may I participate in this meeting?

You may participate in this meeting by following the instructions in this section. To ensure proper receipt by EPA, it is imperative that you identify docket ID number EPA-HQ-ORD-2011-0970 in the subject line on the first page of your request.

1. Oral comments. Requests to present oral comments will be accepted up to Wednesday, January 19, 2011. 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, Wednesday, January 19, 2011, 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, January 19, 2011. 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 section 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, 2011, EPA's Human Studies Review Board will consider scientific and ethical issues surrounding these topics:
—A scenario design and associated protocol from the Agricultural Handler Exposure Task Force (AHETF) describing proposed research to monitor exposure of workers who mix and load pesticides formulated as wettable powders. 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 and load pesticides formulated as wettable powders, and to meet the applicable requirements of 40 CFR part 26, subparts K and L.
—The report of a completed scenario monograph and study reports of five field studies from the Agricultural Handler Exposure Task Force (AHETF) measuring the dermal and inhalation exposure of workers applying liquid spray pesticides to tree or trellis crops using closed cab airblast equipment. The studies were conducted in five states in the U.S. where closed cab airblast equipment is commonly used in production agriculture. 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 workers who apply liquid spray pesticides using closed cab airblast equipment, 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 concerning a Board meeting report, if applicable, can be found at http://www.epa.gov/osa/hsrb/ or from the person listed under **FOR FURTHER INFORMATION CONTACT**.

Dated: January 7, 2011.
Fred S. Hauchman,
Acting EPA Science Advisor.
[FR Doc. 2011-625 Filed 1-11-11; 8:45 am]
BILLING CODE 6560-50-P

Federal Register Notice Correcting Docket Number

[Federal Register Volume 76, Number 12 (Wednesday, January 19, 2011)]
[Notices]
[Page 3134]
From the Federal Register Online via the Government Printing Office [www.gpo.gov]
[FR Doc No: 2011-1062]

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ENVIRONMENTAL PROTECTION AGENCY

[EPA-HQ-ORD-2010-0970; FRL-9254-7]

Human Studies Review Board; Notice of Public Meeting; Correction

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice; correction.

SUMMARY: The U.S. Environmental Protection Agency (EPA) published a document in the Federal Register of January 12, 2011, announcing the January 26, 2011 public meeting of the Human Studies Review Board. The document contained incorrect Docket ID Number.

FOR FURTHER INFORMATION CONTACT: Lu-Ann Kleibacker, 202-564-7189.

Correction

In the **Federal Register** of January 12, 2011, in FR Doc. 2011-625, on page 2107, in the title, correct the "Docket ID No." to read EPA-HQ-ORD-2010-0970. On page 2108, in the first column, correct the "Docket ID No." to read EPA-HQ-ORD-2010-0970.

ADDRESSES: Submit your written comments, identified by Docket ID No. EPA-HQ-ORD-2010-0970:

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-2010-0970. 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 disk or CD-ROM 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. On page 2109, in the first column, correct the "Docket ID No." to read EPA-HQ-ORD-2010-0970:

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-2010-0970 in the subject line on the first page of your request.

Dated: January 13, 2011.
Paul T. Anastas,
EPA Science Advisor.
[FR Doc. 2011-1062 Filed 1-18-11; 8:45 am]
BILLING CODE 6560-50-P

Attachment C

U.S. ENVIRONMENTAL PROTECTION AGENCY
HUMAN STUDIES REVIEW BOARD
JANUARY 2011 PUBLIC MEETING AGENDA

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

Wednesday, January 26, 2011

9:15 AM* **Convene Public Meeting and Review Administrative Procedures –** Jim Downing (Designated Federal Officer, Human Studies Review Board [HSRB], Office of the Science Advisor [OSA], EPA)
Opening Remarks – Warren Lux, M.D. (Director of the Program in Human Research Ethics, OSA, EPA)
Introduction and Identification of Board Members – Sean Philpott, Ph.D. (HSRB Chair)
Welcome and Follow-up on Previous HSRB Recommendations – Mr. William Jordan (Office of Pesticide Programs [OPP], EPA)

Session 1: **Agricultural Handler Exposure Task Force (AHETF) report of a completed scenario monograph and study reports of five field studies measuring the dermal and inhalation exposure of workers applying liquid spray pesticides to tree or trellis crops using closed cab airblast equipment**

9:35 AM **EPA Science and Ethics Reviews –** Mr. Matthew Crowley (OPP, EPA) and Ms. Kelly Sherman (OPP, EPA)
10:35 AM **Board Questions of Clarification** – Sean Philpott, Ph.D. (HSRB Chair), EPA, Principal Investigator/Sponsor
11:10 AM **Break**
11:25 AM **Public Comments**
11:35 AM **Board Discussion – Science**

Charge to the Board:

- Was the research reported in the AHETF completed monograph report and associated field study reports faithful to the design and objectives of the protocol, standard operating procedures, and governing documents?
- Has the Agency adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating exposure of those who apply conventional pesticides with closed cab airblast equipment?

12:35 PM **Lunch**

1:30 PM Board Discussion Continued – Ethics

Charge to the Board:

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

Session 2: Agricultural Handler Exposure Task Force (AHETF) scenario design and associated protocol describing proposed research to monitor exposure of workers who mix and load pesticides formulated as wettable powders

2:30 PM **EPA Science and Ethics Reviews** – Mr. Jeff Evans (OPP, EPA) and Ms. Kelly Sherman (OPP, EPA)
3:00 PM **Board Questions of Clarification** – Sean Philpott, Ph.D. (HSRB Chair), EPA, Principal Investigator/Sponsor
3:30 PM **Break**
3:45 PM **Public Comments**
4:00 PM **Board Discussion**

Charge to the Board:
If the revised AHETF scenario and field study proposal AHE80 is revised as suggested in EPA's review and if the research is performed as described:

- Is the research likely to generate scientifically reliable data, useful for assessing the exposure of handlers who perform open mixing and loading of pesticide end use products formulated as wettable powders?
- Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

5:30 PM Adjournment