Final Minutes of the
United States Environmental Protection Agency (EPA)
Human Studies Review Board (HSRB)
October 25, 2017, Public Meeting
HSRB Website: www.epa.gov/osa/human-studies-review-board

Committee Members:	(See EPA HSRB Members List—Attachment A)	
Date and Time:	Wednesday, October 25, 2017, 1:00–6:15 p.m. EST (See *Federal Register* Notice—Attachment B)	
Location:	Via Teleconference and Webinar	
Purpose:	The EPA HSRB provides advice, information and recommendations on issues related to the scientific and ethical aspects of human subjects research.	
Attendees:	Chair:	Liza Dawson, Ph.D.
	Vice Chair:	Edward Gbur, Jr., Ph.D.
	Board Members:	Jennifer Cavallari, Sc.D., CIH Alesia Ferguson, Ph.D. Kyle L. Galbraith, Ph.D. Walter T. Klimecki, D.V.M., Ph.D. Drue Barrett (Consultant to HSRB)
	EPA:	Michelle Arling (EPA) Timothy Dole (EPA) Timothy Leighton (EPA)
	Study Sponsor:	Has Shaw (American Chemistry Council) Michael Bartels (Dow Chemical Inc.) Brian Lange (Lange Research and Consulting, Inc.) Cameron Lange (Lange Research and Consulting, Inc.) Renee Daniel (Perspective Consulting Inc.) Leah Rosenheck (LR Risk Consulting Inc.)
	Other:	Jonathan Cohen, ICF (EPA contractor) William Jordan (public)
Absent:	Board Members:	Randy Maddalena, Ph.D. Jun Zhu, Ph.D.

Meeting Summary: Meeting discussions generally followed the issues and general timing as presented in the Meeting Agenda unless noted otherwise.

Wednesday, October 25, 2017

Convene Public Meeting

Mr. Tom O'Farrell (Designated Federal Officer [DFO], HSRB [or Board], Office of the Science Advisor [OSA], EPA [or the Agency]) convened the meeting at 1:00 p.m. and welcomed Board members, EPA colleagues and members of the public. He expressed appreciation to the Board members for their service and thanked EPA's Office of Pesticide Programs (OPP) for preparing for this meeting. As DFO, Mr. O'Farrell, under the Federal Advisory Committee Act (FACA), serves as liaison between the HSRB and EPA and is responsible for ensuring that all FACA requirements are met regarding the operations of the HSRB. Also in his role as DFO, he must work with appropriate Agency officials to ensure that all applicable ethics regulations are satisfied. HSRB members were briefed on federal conflict-of-interest laws and have completed a standard government financial disclosure report, which has been reviewed to ensure that all ethics requirements are met.

Mr. O'Farrell informed the Board that the purpose of the meeting was to review the Antimicrobial Exposure Assessment Task Force (AEATF) II Airless Sprayer Study Protocol and finalize the report and minutes from the July 26, 2017 meeting. He mentioned that supporting documents for the meeting were attached to the meeting invite and available on the HSRB web site at www.epa.gov/osa/human-studies-review-board. He noted that the Agenda times were approximate, and the group would strive to allow adequate time for the Agency presentations, public comments and the Board's thorough deliberations.

In accordance with FACA requirements, the Agenda provides for a public comment time, offering the public the opportunity to provide comments to the Board. Mr. O'Farrell announced that he had no public comments, as of the start of the meeting. He stated that members of the public wishing to make a public comment must limit their remarks to five minutes. He explained that the HSRB Chair would call for public comments at the scheduled point in the Agenda.

In accordance with FACA requirements, meeting minutes, including a description of the matters discussed and conclusions reached by the Board, are prepared and must be certified by the meeting Chair within 90 days. The approved minutes will be available on the HSRB website at www.epa.gov/osa/human-studies-review-board. The HSRB also will prepare a final report in response to questions posed by the Agency, which will include the Board's review and analysis of materials presented. The final report will be available on the HSRB website at www.epa.gov/osa/human-studies-review-board. Mr. O'Farrell then turned the meeting over to the HSRB Chair, Dr. Liza Dawson.

Virtual Meeting Operations

Dr. Dawson reviewed the operating procedures for the virtual meeting. She instructed Board members to use the Adobe Connect meetings feature that allows them to raise their hands in the

Adobe Connect website to be recognized by the Chair when offering comments. When voting, the Board members used the polling function in the website to agree or disagree with the proposal.

Introduction of Board Members

Dr. Dawson welcomed the Board members and asked them to introduce themselves, providing their names, affiliations and areas of expertise. Following those introductions, Mr. O'Farrell then asked other attendees to identify themselves.

Opening Remarks

Mr. O'Farrell explained that Dr. Thomas Sinks, Director, OSA, could not attend the meeting to provide opening remarks. He then noted that they would proceed to the next item on the Agenda.

Brief Update on Research Discussed at the last HSRB Meeting

Ms. Michelle Arling, EPA OPP, provided an update on research from previous HSRB meetings. Ms. Arling reported there were no updates on the research discussed at the last HSRB meeting, which was a protocol for an insect repellent study involving the active ingredient IR3535. However, EPA did get an updated standard operating procedure (SOP) related to research discussed at the October 2016 meeting. The HSRB recommended that the Antimicrobial Exposure Assessment Task Force (AEATF) change their SOPs to address two issues. Specifically, HSRB recommended that the AEATF SOP: 1) provide guidance to evaluate study-related adverse events, particularly whether such adverse events would be related or unrelated to participation in the study; and 2) require that medical professionals evaluating such adverse events are independent of the study team. In September, the AEATF sent EPA a revised SOP, and after revising to address a minor comment, the AEATF sent a final version. Ms. Arling shared that final version with the HSRB prior to this meeting.

Dr. Dawson asked whether Board members had any questions or comments about the final version of that SOP, and there were none.

Topic: AEATF II Airless Sprayer Study Protocol

Dr. Dawson explained that two presentations from EPA OPP would be next on the Agenda. She noted that the first presentation would be on background and science assessment, given by Mr. Tim Leighton, EPA OPP Antimicrobials Division. Several others were present to contribute, including Mr. Tim Dole, Certified Industrial Hygienist (CIH), EPA OPP Antimicrobials Division; Dr. Jonathan Cohen, ICF (contractor to EPA to provide support on statistical analysis); and Ms. Leah Rosenheck (consultant to AEATF), QA consultant for the study/protocol. Dr. Dawson noted that Ms. Michelle Arling, EPA OPP, would make the second presentation on EPA's ethics assessment of the protocol.

EPA Science Review Highlights: Presentation on EPA Science Assessment of AEATF II Airless Sprayer Painting Scenario and Protocol

Mr. Leighton began by stating his presentation would provide an overview of the Airless Sprayer Painting Scenario and Protocol. This presentation will include regulatory context, scenario definition, study objectives, surrogate material for testing, study design, measurements, compliance with scientific standards, and recommendations or conclusions.

Mr. Leighton explained that because this study will involve intentional exposure of human subjects, with the intent to submit the resulting data to EPA under FIFRA, it is necessary to fulfill regulatory requirements related to the proposed human exposure. The first regulatory requirement that applies is 40 CFR §26.1125, which requires prior submission of the protocol and supporting documentation. AEATF has already submitted this information to EPA. The second regulatory requirement, which will be concluded today, is 40 CFR §26.1601, which requires review of the protocol by EPA and the HSRB.

EPA decided that a new generation of exposure monitoring was needed to address the limitations of the Pesticide Handlers Exposure Database and Chemical Manufacturers Association (PHED/CMA) databases. For example, one shortcoming is that the existing data is from studies conducted with different measurement techniques. Another shortcoming is the way that the existing whole body data was derived. When EPA OPP brought the need for studies to the FIFRA Science Advisory Panel (SAP) in January 2007, the SAP concurred in the need for new studies for exposure monitoring. The SAP liked the soundness of the "generic principle", which would show trends in exposures. The SAP agreed with the matrix of all potential use categories and exposure scenarios. The SAP also agreed on passive dosimetry techniques and overall study design.

Mr. Leighton described the matrix of all potential use categories and exposure scenarios. The row headings represent the 12 use/site categories, e.g., food handling, medical, material preservatives, and agriculture. The column headings represent the general pesticide application methods, or how people are applying these pesticides, e.g., mop, wipe, pour liquid, spray, brush and roller, and airless spray. EPA has completed work on some of these application methods and some will be addressed in the future. The Airless Spray application method is the subject of this HSRB meeting.

The definition of the Airless Sprayer Scenario is "the application of an indoor latex paint containing an antimicrobial chemical by a commercial painter using an airless sprayer." Included in this definition is the setup and cleanup of painting equipment, and spraying paint (which would include painting walls, ceilings, doors, frames, closets, and shelves). This definition excludes pouring the antimicrobial into the paint, taping, and setup of tarps; any cleanup procedures involving water (to avoid removing residues); and painting with a brush/roller (this scenario was monitored previously). Pouring the antimicrobial into the paint is excluded because this occurs at the manufacturing facility and is an occupational exposure scenario.

Mr. Leighton presented photos of and described the commercial product selected by AEATF: Graco Ultra Max II 695 PC™ Pro. It has a 2 HP motor and generates up to 3,300 PSI. Professional contractors can run two guns and 300 feet of hose for interior residential and light commercial painting. It can be used when painting overhead, including ceilings and doors.

The AEATF II Airless Sprayer study objectives are to: 1) develop more accurate information on exposures to antimicrobials to support exposure assessments for antimicrobial treated paint; 2) satisfy a requirement for new data imposed by EPA's Reregistration Eligibility Decision (RED) documents; and 3) support Registration Review as well as pending and future registrations for various antimicrobial products (e.g., in-can material preservatives). EPA has issued many data call-ins (a data call-in is EPA's regulatory mechanism to require data to be submitted by chemical companies) or paint to satisfy these data requirements.

Surrogate Paint Product

An AEATF task force determined criteria for a surrogate paint product. They wanted material that would be stable and with an appropriately low vapor pressure to make it nonvolatile. Importantly, they wanted a robust and sensitive analytical method because they did not want non-detects, that is, results indicating "no detectable residue," to drive results. They wanted an active ingredient already used in paint and a chemical already registered as in-can material preservative for latex paint. Sherwin-Williams latex paint was selected, in part because this was the same indoor paint as used in the AEATF II brush/roller study.

Propiconazole was proposed as the surrogate test material. Propiconazole is a material preservative used in paints, but not used in textiles or detergents. The EPA Registration Number is 43813-37 and the CAS Number is 60207-90-1. The vapor pressure for propiconazole is 4.2E-7 mmHg at 25°C. Propiconazole can be used in up to 12,000 ppm active ingredient in paint. Finally, although propiconazole can be used in paint (e.g., treated article) without chemical resistant gloves and without respirators, Mr. Leighton noted that issues associated with respirators can get more complex.

Mr. Leighton reviewed existing EPA data on the short-term toxicity of the surrogate test material as well as the long-term endpoint (carcinogenicity). Mr. Leighton also reviewed existing EPA data on dermal absorption that indicated propiconazole was absorbed at approximately one percent (1%).

The AEATF II Airless Sprayer study subject's potential exposure estimates from paint were based on two exposure estimates for the airless sprayer scenario: 1) AEATF II citing EPA's 2011 assessment based on PHED; and subsequently, 2) EPA's updated airless SOP (updated with additional data based on Formella 1995) that changed the unit exposure some. Under the updated unit exposure (UE) approach: Dose = UE mg active ingredient (ai)/lb ai * amount of active ingredient handled (AaiH) lb ai * Abs * (1/kg body weight (BW)). The effect of the change for UEs for airless sprayer was:

- Dermal UE: was 38, but revised to 43 mg ai/lb ai (single layer of clothing, no gloves); and
- Inhalation UE: was 0.83, but revised to 0.56 mg ai/lb ai.

Mr. Leighton explained that after putting all that together, the potential dose/risk estimates for this AEATF II Airless Sprayer study are:

- Margin of Exposure ($MOE_{short\text{-}term}$) = No Observed Adverse Effect Level (NOAEL)/Dose

Dermal = 30 mg/kg / 0.023 mg/kg = 1,300
Inhalation = 30 mg/kg / 0.30 mg/kg = 990

- Margin of Exposure ($MOE_{long\text{-}term\ and\ cancer}$) = NOAEL/Dose
  Dermal = 10 mg/kg / 0.023 mg/kg = 430
  Inhalation = 10 mg/kg / 0.030 mg/kg = 330

Study Design

The AEATF II Airless Sprayer study will be conducted at a single location in Orlando, FL. Study subjects will be painting indoor rooms with an airless sprayer. EPA does not think that exposure will vary geographically. The study will include existing rooms or rooms built in a leased facility. It will include large and small rooms (including ceilings) as well as hallways, closets, doorways, and windows.

Mr. Leighton reviewed the key variables affecting exposure from painting with an airless sprayer. Painting will be indoors, and it will be important to include ceilings, doors, and window/trim because of the need to include overhead painting. For the spray nozzles, AEATF selected five (5) different nozzle tips that will be provided for painting. The nozzle tips were selected based on the tip sizes recommended by the manufacturer for latex paint. The active ingredient concentration will be varied from 1,200 to 12,000 ppm. The amount of paint (hence, duration of painting on the test day) will be varied and this includes the amount of surface area painted. AEATF assumed a maximum of 30 gallons of paint and six (6) hours of painting, plus setup and removal of dosimeters. All clean-up activities will be included (except no water wash down). The study will allow for variability among different subjects, based on their normal painting practices. All test subjects selected will be commercial painters because they typically paint up to 50 gallons with an airless sprayer. The AEATF decided that consumers would not typically use this type of equipment and would need training.

After describing a photo of what the Graco RAC 5 SwitchTip looks like, Mr. Leighton explained those nozzle tips are a Reverse-A-Clean (RAC) SwitchTip that can be easily reversed to clear clogs. The study subjects will have additional nozzle tips to switch out if clogs occur. Mr. Leighton also reviewed a table with specifications for the Graco RAC 5 SwitchTips, noting that the orifice size ranged from 0.015 to 0.021 inches, the swath width ranged from 8-10 to 12-14 inches, and the flow rate in gallons per minute was also provided in the table.

The inclusion criteria are that the test subjects will be professional painters with at least three (3) months prior experience. Each different test subject will represent a monitoring event (ME). The characteristics to capture the high end of exposure include painting indoor rooms that will include painting the ceilings (with the ceiling representing higher exposure because of overhead painting). Professional painters will be used as test subjects because they handle more paint than consumers/homeowners. The amount of paint will be up to 30 gallons at up to 12,000 ppm active ingredient (propiconazole) in paint. Cleanup will be included, except for water that would wash paint from hands.

Mr. Leighton explained the EPA default value for risk assessments is up to 50 gallons of paint, which has been used since the late 1980s to early 1990s, and is based on airless sprayer

specifications. Based on informal discussions with painters over the years, EPA believes the 50 gallon assumption is still reasonable. AEATF did survey some painters for this protocol, and based on that small survey, EPA's 50-gallon default value still seems reasonable. Consequently, the amount of paint being sprayed in this protocol, up to 30 gallons, combined with EPA's ability to extrapolate based on the unit exposure approach, is sufficient.

Mr. Leighton reviewed a summary of the AaiH (amount of active ingredient handled) design and the ME stratification by AaiH. There will be three groups for AaiH, and each group has three (3) MEs for each amount of propiconazole handled:

- For Group 1, 10 gallons of paint sprayed at 1,200 and 12,000 ppm propiconazole concentration;
- For Group 2, 15 gallons of paint sprayed at 1,200 and 12,000 ppm propiconazole concentration; and
- For Group 3, 30 gallons of paint sprayed at 1,200 and 12,000 ppm propiconazole concentration.

Through a total of 18 MEs, anticipated exposure is 2, 3, and 6 hours for the amount of paint handled (maximum of 6 hours will be allowed). Exposure is expected to vary with amount handled, subject-specific behaviors, and characteristics of the sample design.

The random design elements incorporated in the protocol are selection of study participants and assigning the test subjects to three (3) groups and two (2) different propiconazole concentrations. EPA also recommended randomly assigning MEs to sampling dates and rooms painted; however, the sampling dates were deleted from the random design because test subjects would be given calendars to indicate dates they were available for the study.

With respect to painting procedures, Mr. Leighton emphasized that subjects will be told to paint as they normally would do. The AEATF-sponsored researchers will provide a sprayer, multiple spray nozzle choices, spray tip extensions, and rags, etc. The specific tasks performed by test subjects include:

- Opening paint can lids, sprayer setup, etc. (but not masking tape/tarp setup because that will all happen before painting);
- Painting drywall, doors, shelving (walls and ceiling); and
- Cleaning up equipment at the end of the task (excluding washing of spray line/nozzles with water to avoid washing off of the paint on hands).

Measurements

Field measurements will be taken for dermal and inhalation exposure, air temperature and relative humidity, amount of material applied, painting duration, and work observations. Observations will be very important to record subject-specific behaviors. For example, observations would include how workers configure windows and doors to ventilate and if workers use fans for ventilation. Observers will need checklists or another method to obtain consistent observational notes.

Mr. Leighton explained that measurement of dermal residues will be conducted using whole body dosimeters and the same techniques used previously in other AEATF studies. Inner dosimeters will be placed on long-johns and a patch under the painter's cap, which will provide an estimate of dermal exposure. Outer dosimeters will consist of normal work clothing, with a painter's cap, to provide an estimate of protection provided by a single layer of clothing. The test subjects will have a hand wipe/wash at the end of the task and at breaks. They will also have a face/neck wipe at the end of the task and at breaks. Mr. Leighton briefly noted that preliminary results of the Hand Wash Efficiency (HWE) study for the 1,2-benzisothiazoline-3-one (BIT) active ingredient in AEATF II Brush/Roller Painting Scenario and Protocol may be bridged to propiconazole. EPA will make a final determination about whether the data can be bridged after the final HWE study for BIT study is submitted and reviewed.

For measurement of inhalation exposure, two (2) personal air samplers will be worn. The OSHA Versatile Sampler (OVS) tubes measure total inhaled residues. The parallel particle impactors (PPIs) with PVC filters measure respirable particles (50% cut point 4 μm, particles above 4 μm are retained by impaction, while smaller particles continue to the PVC filter behind the impaction substrate). The PPI sampler is attached to an air sampling pump worn on a belt. Subjects will wear the OVS tube, which has air drawn into the larger orifice through the filters and two (2) beds of sorbent. Mr. Leighton showed images of how the PPI samplers are used.

Analysis

Mr. Leighton briefly reviewed the matrices for analysis: whole body dosimeters, painter's cap, cap patch, hand wipes/washes, face/neck wipes, and air samples. Next, Mr. Leighton presented a table of Fold Relative Accuracy, which was provided as information to determine whether sample size was large enough to meet the 3-fold accuracy benchmark.

Compliance with Scientific Standards

The Airless Sprayer Painting Scenario and Protocol has addressed the technical aspects of applicable exposure monitoring guidelines, specifically, EPA Series 875 Group A -Applicator Monitoring Test Guidelines; OECD Applicator Guidelines; and Good Laboratory Practices (GLPs) (40 CFR Part 160). All previous comments by EPA have been satisfactorily addressed.

EPA has provided several new recommendations:

- EPA recommends randomly assigning MEs within each paint volume group (Groups 1, 2 and 3 for 10, 15 and 30 gallons, respectively) to rooms painted;
- EPA wants to provide clarity to the test subjects on the logistics of stowing the sprayer equipment if not washed with water (and thus still covered in paint);
- EPA wants to better capture in the observational notes if subjects dilute paint with water, and be able to account for the dilution; and
- EPA believes it appears sound to incorporate the bridging rationale to use the existing HWE study for BIT rather than performing a separate HWE for propiconazole , however, final judgement will be made once the BIT study is submitted and reviewed.

In conclusion, Mr. Leighton stated EPA's finding that the Airless Sprayer Painting Scenario and Protocol is likely to yield scientifically reliable information, satisfying the following criteria:

- It would produce important information to fill an identified regulatory need;
- This need cannot be addressed except by research with human subjects;
- It has a clear scientific objective; and
- The study design should produce data adequate to achieve the objective.

EPA Science Review: Board Questions of Clarification

Dr. Dawson thanked Mr. Leighton and asked for any questions of clarification from Board members about the presentation.

Dr. Klimecki wanted to get clarity about the evolution of margin of exposure (MOE) in EPA's risk assessments for propiconazole. Dr. Klimecki understood that the 2006 evaluation conducted for propiconazole registration had recommended that the allowable level of the active ingredient be reduced (from 0.35% to 0.125%) based on the MOE at that time. Dr. Klimecki also understood this recommendation was based on the assumption of dermal absorption for propiconazole. Subsequently, Janssen Pharmaceuticals provided absorption data that EPA accepted as valid, and Janssen's data indicated that absorption was around one (1) percent. Dr. Klimecki understood that EPA did an updated risk assessment because that changed the MOE. Dr. Klimecki asked if that was roughly correct.

Mr. Leighton stated that was roughly correct. Janssen Pharmaceuticals did a study of propiconazole in paint that showed absorption was actually one (1) percent, but emphasized that they only studied propiconazole used in paint, and it was not the liquid propiconazole formulations.

Dr. Klimecki noted that part of what confused him in the documentation supplied to HSRB was a letter from an EPA official advising Janssen of the modification to the registration, which indicated the original 2006 risk assessment assumption was 100 percent absorption. But the actual 2006 re-registration document stated the assumption was 40 percent absorption, and the Janssen data showed one (1) percent was a more realistic value. Dr. Klimecki wanted clarification from EPA scientists that the most accurate values for absorption were used to determine the MOEs in this study.

Mr. Leighton believed he did the last EPA assessment that used the one (1) percent dermal absorption. Mr. Leighton had a letter from Mark Harman of EPA to William Goodwine of Janssen Pharmaceutical dated July 9, 2012. The letter states that the 2006 RED used 100% dermal absorption. However, Table 3 of the 2006 RED shows that EPA used 40% dermal absorption for assessing propiconazole. Table 5 in this RED also includes the toxicity endpoints for triazole conjugates and the dermal absorption for the triazole conjugates is listed as 100%. EPA staff believe that in 2012 Mark Hartman cited the dermal absorption value from the incorrect table when writing the letter.

In summary, the 2006 RED used 40% dermal absorption for propiconazole. Subsequent to the RED the registrant submitted a new dermal absorption study using propiconazole in paint to

show the paint matrix's effect on dermal absorption. Based on this more recent study, the new estimate of dermal absorption of propiconazole in paint is 1%.

Dr. Klimecki asked about the assumption about wearing PPE in EPA's 2011 updated risk assessment using the one (1) percent dermal absorption to calculate MOE. Mr. Leighton did not have the EPA 2011 assessment cited by the AEATF in front of him but no respirators or gloves were used. The 2011 EPA assessment was the reevaluation of propiconazole in paint using the newly submitted dermal absorption study showing 1% dermal absorption from paint matrix.

Dr. Klimecki raised to the HSRB's and EPA's attention a 2015 EU study that showed MOEs for propiconazole for professional paint applicators without PPE were around six (6) for a product that had 0.3 percent propiconazole. If EPA's MOEs are not assuming PPE, then it seemed a big difference in the MOEs between that 2015 EU study and EPA's risk assessment.

Mr. Leighton stated that Mr. Tim Dole had just given him information about assumptions from EPA's assessment, which was no gloves and no respirators. Mr. Leighton would have to look at the EU study for information about their dermal unit exposures and dermal absorption.

Dr. Klimecki did not know the correct order of events in order to evaluate these seemingly big differences in MOE, and recognized assumptions that the 2015 EU study was using could be very different from assumptions used by EPA.

Mr. Leighton stated that EPA used a short-term NOAEL of 30. Dr. Klimecki saw that the EU study used a short-term NOAEL of 30, and said he will forward the EU study to EPA.

Dr. Cavallari had a question about use of professional painters versus consumer users. Dr. Cavallari noted that the protocol indicated there might be an underestimation of exposure through the use of professional painters. Dr. Cavallari was concerned that consumer painters may have more dermal exposure from direct contact with paint or splashing. After noting that the use of professional painters was part of the scenario definition, Dr. Cavallari asked whether this had already been thoroughly discussed in deciding on the scenario definition.

Mr. Leighton stated it had been discussed thoroughly. EPA must conduct an assessment both for commercial painters and consumers (for brush rollers, which consumers typically use). EPA delineates by unit exposures and different amounts of paint: 50 gallons for airless paint sprayers for commercial painters and 15 gallons for brush rollers for consumers/homeowners. Airless paint sprayers are typically used only by commercial painters.

Dr. Cavallari noted that the charge to the Board was more generic and did not specify assessing exposure for commercial or professional painters.

Mr. Leighton stated that EPA was only developing a unit exposure for airless paint sprayers. EPA decided that commercial or professional painters would best represent exposure for airless paint sprayers.

Dr. Dawson asked if it would it be correct to say that EPA and AEATF viewed commercial versus consumer users to have about the same exposure per unit of active ingredient handled, and whether the results could be extrapolated. Mr. Leighton stated that EPA would assess consumer users at 15 gallons and commercial users at 50 gallons, so the commercial users would be handling three (3) times more. Dr. Dawson asked whether the amount of exposure per unit handled could be higher for consumers, for example, if consumers were much sloppier at painting. Mr. Leighton explained that commercial painters are the driver because their exposure is three (3) times higher based on extrapolating the amount of active ingredient handled (AaiH) from using larger volumes of paint. Mr. Leighton also noted that airless paint sprayers might be more risky for consumers in this study if they did not know how to operate the equipment.

Dr. Gbur asked if EPA has any hard data on how much paint consumers use. Mr. Leighton stated that 15 gallons was enough to paint a house.

Dr. Ferguson had read the survey of professional painters over the weekend and was concerned that survey included only seven (7) individuals and was not well designed. Dr. Ferguson believed that EPA will probably not capture differences in work practices for the high-risk professional painters using large volumes of paint (100-200 gallons working 10-12 hours per day). Mr. Leighton conferred with Mr. Dole and stated that very large paint jobs using nozzles with the widest swaths, such as when painting an oil storage tank or warehouse, would not be using a water-based latex paint that needed an antimicrobial product as preservative. Dr. Ferguson was still concerned about adding clarity about how well this study represented large commercial painting companies that might be using 100-200 gallons.

Dr. Cavallari noted that different nozzles and wands will be provided to subjects, and she asked whether subjects will be able to change them out. Mr. Leighton stated it will be up to the painters about whether to change out nozzles or wands during painting. After conferring with Mr. Dole, Mr. Leighton explained that painters will change out nozzles as they wear out, or when they move to different areas that might need a different swath width (e.g., from ceiling to door).

Dr. Cavallari asked a question about room size because EPA suggested randomizing based on room size and shape. Dr. Cavallari was not clear whether the subjects will be told to use up all paint or to achieve a certain surface area of painting for a certain number of gallons of paint. Mr. Leighton believed that subjects will be given enough paint to cover the surface area provided and then allowed to decide how much paint to apply using their normal work practices.

EPA Ethics Review Highlights: Presentation on EPA Ethics Assessment of AEATF II Airless Sprayer Painting Scenario and Protocol

Ms. Michelle Arling, Human Research Ethics Review Officer, EPA OPP, began by stating that the ethics review highlights would include: value to society, recruitment, subject eligibility, consent process, risks and risk minimization, benefits, risk-benefit balance, respect for subjects, independent ethics review, EPA recommendations, and ethical standards with respect to applicability and compliance. Reliable data on potential dermal and inhalation exposure are needed to support EPA's exposure assessments and have a value to society because many professional painters and consumers apply paint that contains antimicrobial products.

Subjects will be recruited through three (3) methods: two (2) newspapers (both printed and online versions), radio spots in English and Spanish, and flyers posted in paint stores after requesting permission to post them. The ads will be run concurrently in all mediums for a week at a time, until at least 20 eligible candidates have agreed to attend a consent meeting. Ads in English and Spanish will briefly describe the study and provide information on who to contact if interested in participating. Interested candidates will be informed about the study by phone, screened for eligibility using a pre-determined script, and invited to meet with study staff for an in-person consent meeting. Ads will be run again if an insufficient number of subjects are found eligible to be enrolled.

EPA determined there was no evidence that targeting recruitment of potential subjects from a vulnerable population existed, because the study was targeting professional painters. Because recruitment will be conducted through newspapers, radio, and flyers–not employers–the study will minimize potential for coercion/undue influence on employees. Recruitment materials and meetings will be conducted in English or Spanish, depending on each interested person's preference.

For subject eligibility, the inclusion criteria are: 18-65 years old, good health, three (3) months experience using an airless sprayer professionally within the last five (5) years, and the ability to speak and read English or Spanish. The definition of "good health" is the ability to lift 5-gallon buckets of paint, and spray up to 30 gallons of paint while wearing respirator and eye protection. Interested persons cannot participate, or will be excluded, if: 1) they are pregnant or nursing; 2) have skin conditions on hands, face, or neck; 3) have allergies/sensitivities to chemical-based and/or latex products; 4) are unwilling to participate without gloves; or 5) are an employee or spouse of an employee of AEATF, Sherwin Williams, American Chemistry Council, or the research company.

The consent process will consist of an in-person meeting with the potential subject and researcher, although potential subjects will be invited to bring a spouse or partner. This meeting will be conducted in English or Spanish, depending on the language preferred by the candidate. The consent meeting covers: study design, eligibility criteria, compensation, potential risks and discomforts, treatment and compensation for injury, freedom to withdraw without penalty/forfeiting benefits, and the process for pregnancy testing for women on the study day. Paint and antimicrobial labels and Safety Data Sheets (SDSs) will be available during the consent meeting, and copies will be provided to candidates upon request. After conducting the consent meeting and prior to enrolling a subject, the researcher will ask a series of open-ended questions to ensure comprehension of the materials covered, and if any questions are not understood the researcher will go over them again. Ms. Arling read this series of questions. Candidates can either take the consent form home and think about whether to enroll, or decide to enroll immediately after this in-person consent meeting.

Interested and eligible candidates who have completed a consent form approved by an Institutional Review Board (IRB) then fill out a Subject Qualification Worksheet. Ms. Arling reviewed Part 1: Qualifications Questions portion of this Subject Qualification Worksheet and explained that Part 2 asks for personal information.

The AEATF II Airless Sprayer Painting Scenario and Protocol evaluated risks and included measures to minimize identified risks. Exposure to the chemicals (latex paint, propiconazole, and rubbing alcohol) will be minimized through the eligibility criteria, which includes excluding individuals with skin conditions, and by wearing protective gear such as two layers of clothing and safety glasses. The physical risks associated with painting activities will also be minimized by recruitment of individuals in good health and with related painting experience. The protocol will minimize the risks of heat-related illnesses by scheduling the study for a cooler period in Orlando, FL, and other measures such as providing subjects with water and breaks at any time they are requested. The risks associated with air sampling devices are minimal. Psychological risks will be minimized by having a private area to change clothing and by having a researcher of the same sex assist with donning and doffing PPE.

With respect to benefits, Ms. Arling noted that this research will not offer any direct benefit to subjects. The research will provide reliable data about dermal and inhalation exposure leading to improved occupational and residential exposure and risk assessments. EPA will use the data for antimicrobial product registrations, and society will benefit from higher quality exposure and risk assessments for antimicrobial products.

Ms. Arling stated that the risks have been effectively minimized. The risks to subjects will be low, and those risks are considered reasonable in light of potential societal benefits.

Respect for Subjects has been incorporated, as listed below:

- Participants are free to withdraw at any time for any reason, without penalty or forfeiting benefits.
- Proposed payments to subjects are reasonable ($20 for consent meeting; $200 for enrolling in the study as a subject or alternate), and considered adequate compensation (not too high or too low).
- Participant privacy will be respected, for example, any photographs will not show subjects' faces or identifying features (e.g., tattoos) and all references to subjects in publications and reports will be anonymized.

An independent ethics committee has reviewed the protocol. Schulman IRB reviewed and approved the following study/protocol materials: Protocol dated 7/21/17, advertisements (English and Spanish), recruitment scripts (English and Spanish), informed consent form (English and Spanish), and Subject Qualification Worksheet (English and Spanish). Schulman IRB is registered with OHRP, has AAHRPP accreditation, and is independent of the investigators. Schulman IRB will review all the study/protocol materials again before the research begins.

EPA has provided some recommendations for the study/protocol:

- EPA recommended that researchers enroll subjects who already wear a filtering face piece or half-face respirator while using an airless sprayer, which will allow subjects to use a respirator they are familiar with. EPA did not recommend that researchers require subjects to provide records for respirator fit testing.

- EPA recommended adding risks associated with wearing a respirator and how they will be minimized to the protocol and consent materials.
- EPA recommended adding risks associated with unanticipated release of confidential information and how they will be minimized to the protocol and consent materials, which will minimize breach of confidentiality.
- EPA requested that researchers have available at consent meetings a list of AEATF and American Chemistry Council member companies in order to exclude employers associated with those entities.
- EPA requested that AEATF clarify the amount of compensation for alternates and how they will receive compensation.
- EPA questioned the purpose of wall sampling, and recommended an updated protocol prior to initiating research with a rationale and additional methods for taking wall samples.
- EPA recommended providing subjects with booties to protect shoes from paint spray, but after AEATF provided more information, they decided to withdraw the recommendation for subjects to use booties because it would be an abnormal work practice for professional painters and might cause subjects to slip and fall while using the airless sprayer equipment.

Ms. Arling emphasized that this 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 this research are 40 CFR 26, particularly subparts K and L. Ms. Arling also explained that the Attachments 2-6 to the EPA Review, which were provided to the HSRB, contain point-by-point evaluations of how the study/protocol addresses the requirements of 40 CFR 26 subparts K and L

Ms. Arling stated that according to EPA's review, with the recommendations of EPA and the HSRB incorporated, the study/protocol would be in compliance with applicable ethical standards. The requirements of §26.1111, §26.1116, and §26.1117 have been met. The study/protocol has been submitted to IRB, HSRB, and excludes pregnant women and children. Moreover, the requirements of §26.1125 and §26.1203 have been met.

EPA Ethics Review: Board Questions of Clarification

Dr. Dawson thanked Ms. Arling and asked for any questions of clarification from Board members about the presentation.

Dr. Gbur asked to go back to Slide #54. Dr. Gbur was concerned about how the second bullet read on Slide #54, because the study is not collecting data on residential exposure and only sampling part of the population relevant to the product being studied. This second bullet on Slide #54 stated: "Reliable data about dermal and inhalation exposure leading to improved occupational and residential exposure and risk assessments." Ms. Arling stated that EPA could be more explicit for that second bullet.

Dr. Galbraith asked whether all women would be required to take a pregnancy test. Ms. Arling said yes, and asked Ms. Rosenheck to confirm. Ms. Rosenheck confirmed that the protocol now states that all women will take a pregnancy test.

Dr. Galbraith asked if an individual's name and contact information would be retained if they had called and expressed interest in the study, but then decided they were not interested. Ms. Rosenheck explained that when an individual calls the phone number in response to an ad that their name and phone number would be kept on a sheet, which will also record whether they meet the eligibility criteria. If they decide they are not interested, that will be recorded with their name. That sheet is part of the confidential file.

Dr. Galbraith noted the ads do not mention the need for a government-issued photo ID, but that is part of the protocol. Dr. Galbraith recommended that the ads include this requirement in order alert potential subjects up front.

Dr. Cavallari wanted to check whether most employees who were part of a larger organization would have an employer-supplied respirator. Dr. Cavallari also asked why the recruitment materials did not mention the need to bring a respirator. Ms. Arling stated that because the discussion about respirator use has not been finalized, the language for the consent form and recruitment materials has not been updated. AEATF will update the recruitment materials once the final parameters for subjects' respirator use is agreed upon.

Dr. Cavallari asked for clarification if the subject is told to bring a respirator, whether that would be their employer-supplied respirator. Dr. Cavallari expressed concerns that employer-supplied respirators might need to stay at the employer workplace.

Mr. Dole noted that painters often move from job site to job site, and often take their employer-supplied respirators. Dr. Cavallari asked whether those respirators are equipment that is the property of the employer. Ms. Arling mentioned that EPA had not considered that employers may not allow an employee to take their employer-supplied respirators, but would take this concern under advisement. Dr. Ferguson asked why EPA could not supply the respirators to subjects. Ms. Arling explained that AEATF is conducting the study and would be responsible for providing any protective equipment. Further, Ms. Arling noted that conducting respirator fit testing is complex and based on conversations with AEATF, EPA understood that painters would have their own respirators and could bring them. Ms. Arling also stated that if subjects brought respirators that would not impose additional costs on the subject or the study sponsor.

Dr. Klimecki stated that he understood the desirability of recruiting painters from large and small employers. Dr. Klimecki questioned how EPA would address whether a respirator was being used appropriately (e.g., if the subject has a full beard), even if they do not bring a respirator and instead might use a study-provided respirator (e.g., N95).

Ms. Rosenheck stated that was a good question and explained that was the reason that EPA decided to change the protocol. Respirators were originally in the protocol, but then the question came up about fit testing. The decision was to recruit individuals who already use a half-face

respirator at their job and assume such individuals would know how to use their respirator properly.

Dr. Klimecki understood the issue of fit testing and suggested that EPA might want to provide a list of best practices.

Dr. Barrett (HSRB Consultant, CDC) asked whether subjects will be required to be a resident of Orange County, FL, and if yes, that residency requirement should be clarified in the recruiting materials. Ms. Rosenheck stated the answer is no, but acknowledged that information had come from a previous study and would be deleted from the protocol and related materials.

Dr. Barrett expressed concerns about the reading level and the chemical terms in the recruiting materials. Dr. Barrett questioned whether the population being recruited for this study would be able to understand that terminology. Ms. Rosenheck suggested that would need additional review. Dr. Barrett added that she had already provided detailed questions and comments to Mr. O'Farrell.

Public Comments

Dr. Dawson asked whether there were any public comments.

Mr. William Jordan commented about whether this study will provide adequate information to understand the principal variables to understand exposure. Mr. Jordan specifically referred to Slide #21: "Key Variables Affecting Exposure from Painting." Mr. Jordan commented that two principal determinants are individual behavior and the amount of active ingredient. He agreed with EPA's decision to include painting ceilings; however, he believed that the room structure itself would have an impact (e.g., louvered doors). Mr. Jordan was concerned about how individual behaviors might change if it gets too warm, and how that might affect dosimeter measurements. Mr. Jordan was concerned that exposure from cleanup was not included in the study, and believed that looking at just painting will underestimate exposure.

Dr. Dawson asked if there were any other public comments, and there were none. Dr. Dawson announced a 15-minute break.

Board Discussion

Board Discussion—Science

Dr. Dawson asked discussants Dr. Jennifer Cavallari and Dr. Alesia Ferguson to provide their comments. They agreed that Dr. Cavallari would lead the discussion about scientific review.

> **Charge to the Board - Science:**
> ***Is the protocol "A Study for Measurement of Potential Dermal and Inhalation Exposure During the Application of Paint Containing an Antimicrobial using an Airless Sprayer" likely to generate scientifically reliable data, useful for assessing the***

exposure of those who apply products containing antimicrobial pesticides as preservatives using an airless sprayer?

Dr. Cavallari and Dr. Ferguson were the assigned discussants for the science review. Dr. Cavallari provided a summary of their comments to the HSRB. Dr. Cavallari was thankful for a thorough protocol. Dr. Cavallari emphasized the need to assess whether the 18 monitoring events as designed would provide broad and representative exposure data. She also recommended making sure the variables that are adjusted during the protocol captures the full range of use patterns and application methods and will provide good data. Dr. Cavallari mentioned that they thought about dermal exposures and inhalation exposures during the scientific review. They also thought about the use of professional painters as subjects, and whether that might result in underestimation of potential dermal exposures because consumers would be less experienced than professional painters.

Dr. Cavallari questioned how well extrapolation to higher paint volumes would work, starting with the assumption that consumers use 15 gallons. She asked whether a three (3) times higher exposure volume for professional painters is enough information to develop an adequate extrapolation.

Dr. Cavallari stated that one feature of the protocol she was concerned about was the volume of paint used. Dr. Cavallari wanted justification for whether 50 gallons per day was possible to use in this study, and she referred to page 12 of the protocol. This part of the protocol states that Three discrete volumes of paint will be sprayed in the study: 10, 15, and 30 gallons, with 6 MEs assigned per volume. According to interviews with the seven commercial painting companies, on average a painter will spray 28 gallons per day, with a range from 12 to 50 gallons; the 90th percentile was 41 gallons per day (Appendix B). Companies with 4 employees or less typically spray 15 to 40 gallons of paint in a day. The exposure data generated from this study will be normalized by pounds of active ingredient handled, and can be extrapolated to the EPA daily default for airless spraying of 50 gallons per day for assessing occupational risks. Another feature of the protocol that raised concerns was room size. She noted that a large space may be unrealistic. Dr. Cavallari also suggested that it may be helpful to have a recommended target application rate consistent with the paint manufacturer's recommendations.

Dr. Cavallari was concerned about the use of windows and fans, and she referred to page 31 of the protocol. Specifically, Dr. Cavallari questioned whether air flow velocity will be measured. She suggested that a method to characterize ventilation will be necessary to understand if conditions are realistic.

Dr. Cavallari noted that the questions that she and Dr. Ferguson had about spray nozzles and wands were adequately captured in the earlier discussion.

Dr. Ferguson explained that they had concerns about paint viscosity. She noted that paint manufacturers have different formulations. Dr. Ferguson suggested that the study should specifically address the typical viscosity of paint and relate viscosity to release from the nozzle, which might help with extrapolation to other scenarios.

Dr. Cavallari agreed with volume of paint used for the 10, 15, and 30 gallon paint volume groups, but suggested additional justification be included in the protocol document. . She suggested considering additional details on target coverage of paint in terms of gallons per square foot. Dr. Cavallari recommended that the protocol randomize other structures, such as shelves and closets, and in addition to ceilings. She also recommended that the protocol should take into account ventilation as a factor influencing exposure, especially if subjects open windows or use fans.

Dr. Ferguson believed that a separate study could be conducted regarding the nozzles. She agreed with identifying the five typical types of nozzles in the study, but was concerned that there was no control over which nozzles would be chosen by painters. Dr. Ferguson was concerned that with so many different work behaviors that the subjects could use, that it was possible some nozzle types might not be chosen during painting. Dr. Cavallari added that it was important that the study include both ceilings and walls when subjects were painting.

Dr. Ferguson discussed that more documentation would be good to include in the protocol. One recommendation was to provide 2-4 hours of training on how to record field/observational notes. For field notes, she mentioned that some observations that could be documented were how far painters were away from the walls and whether painters were bending over. She emphasized that there were many other work practices that could be recorded in field/observational notes.

Dr. Cavallari mentioned work practices related to dermal exposures, especially with the use of rags to wipe up spills. She asked whether such work practices would reduce dermal exposures. Dr. Ferguson asked whether rags will remove paint from the hands, and emphasized that it was important to recognize all factors that affect exposure or potential exposure. Dr. Cavallari noted that she was not sure whether the protocol required subjects to wash hands before they started to paint.

Dr. Ferguson had asked EPA to explain the purpose of the wall wipes and EPA deferred to the AEATF.

Dr. Cavallari and Dr. Ferguson noted that they also had questions on ethics. Dr. Dawson asked them to mention those ethics questions. Dr. Cavallari was concerned about respiratory protection, especially the idea that subjects should bring their employer-supplied respirator. She emphasized it was important to mention respirators in the recruitment materials. Dr. Cavallari asked whether earplugs would be required and noted that OSHA requires two (2) forms of hearing protection. She stated that small ladders are a hazard and should be mentioned in the consent form.

Dr. Cavallari stated they had concerns about the videotaping, and asked whether subjects would have any say about videotaping. Dr. Cavallari stated they were also concerned about whether alternates would be taken to the test site on the day of the study, and concerned about provision of snacks.

Dr. Cavallari was also concerned about what would happen if a subject does not know how to answer the question about allergies. Dr. Ferguson added that language concerns might arise with respect to the allergy questions in the screening process to determine eligibility for the study.

Dr. Dawson asked the discussant Dr. Gbur to provide comments about the statistical review.

Dr. Gbur began his comments by acknowledging that practical and ethical constraints can create small sample sizes. Dr. Gbur was concerned that data were being collected about a specific population and extrapolated. He recommended it was better to assume data from the study allows inferences to be made about professional painters but not necessarily other groups.

Dr. Gbur referred to page 12 of the EPA Science and Ethics review memo submitted to the HSRB that describes the main statistical model, and noted that all three (3) paint volume groups will be put together and are assumed to have a slope of one. This is equivalent to the assumption of proportionality. His question was: what is EPA fitting there? Dr. Gbur acknowledged that while some of the analysis regarding fitting a model is subjective. He emphasized that it was important to not automatically assume a log-log slope of one.

He noted that statistical models will usually start out complex and are simplified as much as possible during analysis. Dr. Gbur advised that the researchers should only consider fitting the data to a log-log slope of 1 after initial analysis of the statistical model.

In terms of straight line model performance, Dr. Gbur recommended looking at the pattern in residuals. He suggested analyses to determine if residuals were related to air temperature, relative humidity, or other potential covariates (e.g., height of ceiling).

Dr. Gbur suggested using Information Criteria; Akaike's Information Criterion (AIC or AICCC) or a Bayesian Information Criterion (BIC), to compare statistical models as an alternative approach. These models are based on a likelihood approach to evaluating the fits of competing models.

Finally, Dr. Gbur referred to page 41 in Attachment #2 of the EPA Science and Ethics review memo submitted to the HSRB, and read a portion that addressed the idea that the statistical power was 100 percent. Dr. Gbur emphasized it was important to carefully review this, as an assumption of 100% statistical power would indicate a 0% probability of making a type II error (i.e., not rejecting a false null hypothesis), which seems unrealistic.

Dr. Dawson opened the discussion to other comments from Board members. Dr. Dawson began this open discussion period by categorizing two main trends from the discussants: 1) evaluate the use of professional painters and whether that is representative, and 2) evaluate whether all of the variables that affect exposure are included and how to analyze them. Dr. Dawson asked whether the Board members agreed with those two main trends.

Dr. Cavallari reminded everyone that EPA mentioned this study was a starting point, and if large variations were found then more study would occur. Dr. Gbur agreed that this study was only a starting point, and if necessary, the study could be modified or go in a different direction. He

believed that the major question would be what patterns are found in the study data, and then that leads to the question of why and whether something was missed in the data. Dr. Gbur emphasized that this study will not be an end point, but a starting point.

Dr. Gbur stated that he agreed with the two main trends.

Mr. Leighton explained that EPA intentionally tried to diversify the study for the 18 monitoring events. For example, the study will compare whether the subjects used rags to clean hands more often or painted different size rooms. Mr. Leighton noted that EPA wanted to get all variables that might affect exposure.

Dr. Gbur mentioned that EPA's regulatory authority cannot control behavior for painting. Mr. Leighton explained that because antimicrobials used to preserve paints in cans are considered "treated articles" rather than pesticides under FIFRA, EPA cannot include requirements for users, e.g., gloves, respirators, use rates, the way they could on a pesticide label.

Mr. Leighton stated that Dr. Gbur's comment that data were being collected about a specific population—professional painters—and that the study was only related to professional painters was a good point. Consumers will use paint much less frequently than professional painters. Mr. Leighton agreed with Dr. Gbur's characterization that this study is about professional painters. Dr. Dawson recommended that EPA needs to note the limitations of studies.

Dr. Ferguson commented that if there are multiple variables for dermal exposure, the study may not be able to determine which of those variables drove subject's dermal exposure higher. Dr. Ferguson suggested that both quantitative and qualitative data will be important when evaluating dermal exposure.

Mr. Leighton explained that if EPA gets a wide range of results, then it is possible that more research will be needed and more data collected. He noted that the study has a small sample size and many variables are included. If one of the covariates makes the range much higher than anticipated, that will lead EPA to ask if more research is needed.

Dr. Dawson asked if the Board members had any more comments. Dr. Dawson stated she was clear about what Dr. Gbur was recommending. Dr. Dawson noted that Dr. Cavallari and Dr. Ferguson made a lot of suggestions, but was not sure how many were recommendations to change the protocol versus an interesting idea to think about.

Dr. Cavallari acknowledged that she made a lot of suggestions, but explained they were ideas for consideration, not recommendations about the protocol. Dr. Cavallari stated one possible recommendation for the protocol related to airflow velocity, which was mentioned on page 31 of Volume 2 of the AEATF protocol but not again, so that portion of the protocol was unclear.

Mr. Dole explained that for the painting scenarios in the study, there will be random ventilation instead of regular ventilation. The study scenarios will not include regular ventilation, such as exhaust points with a building system. Because the study uses random ventilation, it would be difficult to measure ventilation rates with standard equipment.

Dr. Ferguson asked for clarification about whether the researchers planned to measure ventilation. Ms. Rosenheck stated they did measure ventilation in two previous studies, but those studies involved a controlled situation. In this study, painters will be moving from room to room. Some painters may choose to put fans or blowers at doorways to move air out of rooms; however, painters may or may not take fans or blowers with them as they move around. Ms. Rosenheck stated it would be very hard to collect meaningful airflow rates.

Dr. Cavallari agreed that there may not be a good way to measure airflow, and stated that this was just a suggestion and not a recommendation. Dr. Ferguson noted some programs exist to model airflow based on using a fan in a room, but Dr. Ferguson agreed that measuring ventilation was only a suggestion and not a recommendation. Dr. Dawson confirmed that the discussion about airflow and ventilation was only a suggestion for clarification to the protocol and not a recommendation for revision.

Dr. Dawson asked the Board members to discuss nozzles next. Dr. Ferguson stated that additional explanation was needed in the study's tables to clarify the paint viscosity issue. Those tables are confusing because they are not referring to paint, and those tables could be more explanatory. Dr. Cavallari agreed.

Dr. Ferguson described the issue that very high end exposures are possible (if professional painters are using 100-200 gallons per day), and also noted it was a suggestion to clarify that such exposures will not be studied. Mr. Dole stated he had been looking at the Graco Manual for airless sprayers, which mentions a paint usage rate of 5 gallons per hour in an example of how worn nozzles affect painting. Mr. Dole stated that 100-200 gallons per day does not seem realistic, even for professional painters. Dr. Ferguson suggested clarifying that the study does not address large painting companies that might use 100-200 gallons per day.

Dr. Dawson thanked Dr. Ferguson for thoughtful points, and reminded Board members it was necessary to differentiate what was simply a clarification or idea to remember for the future, versus a recommendation to revise the protocol. Dr. Dawson also reminded the Board members that HSRB must be clear about recommendations in the Board's responses to charge questions.

Dr. Ferguson noted again that the high-risk group (100-200 gallons) is not included in the study.

Ms. Rosenheck asked the Study Director for more information about the survey questions asked to the painters earlier. Mr. Brian Lange, Study Director, explained the survey of painters was designed to gain more understanding of what a typical day was for professional painters. Mr. Lange noted that painting can be a large operation, but spraying such a large amount of paint would be very unusual.

Dr. Ferguson asked for clarification that high volume scenarios are not included in the study. Dr. Dawson confirmed that Dr. Ferguson's comment was a clarification point and not a recommendation. Dr. Cavallari added that most of her comments were clarifications and not recommendations to revise the protocol.

Dr. Dawson stated that one action item would be documenting the various work practices, and asked the Board members if there were any other action items.

Dr. Ferguson asked the Board members whether they wanted clarification about wall wipe samples. Ms. Rosenheck explained the main reason that wall wipe sampling was in the document, was simply that it was part of an earlier protocol that was used as a template for developing this protocol. Although the researchers discussed taking wall wipe samples in this protocol, she would agree with removing the wipe samples. Ms. Rosenheck explained that one complication is that Health Canada is interested in wall wipe sample results.

Dr. Ferguson stated the purpose of wall wipe sampling is not clear and suggested removing wall wipe samples because it was confusing. The Board agreed that wipe samples should be removed from the protocol if not necessary.

Dr. Ferguson mentioned several other comments: 1) add a few sentences on personnel training about capturing the work practices in the field/observational notes; 2) show EPA how the researchers will collect data on the form; and 3) add a wait time before discarding the researcher's gloves, because those gloves would have residues and the dosimeters may still have wet paint. Ms. Rosenheck explained the protocol will minimize the researcher's handling of clothing and will include not touching clothing where clothing is contaminated with paint along with putting clothing on hangers. Ms. Rosenheck added that the protocol could also include leaving dosimeters on the clothing on hangers for a specified period of time. That would alleviate the concern about transferring paint to the researcher's gloves. Dr. Ferguson agreed with that approach.

Dr. Dawson stated that the Board members should determine their response to the charge question. Dr. Cavallari asked about the issue of professional painters versus consumers. Dr. Dawson reminded Board members that the charge question said "those who apply products" and the Board cannot change the charge question. Dr. Dawson proposed the following: "The study will generate reliable data for assessing the use of these products by professional painters," and perhaps the Board could add caveats about the applicability of the data to consumers.

Dr. Dawson asked the Board members for their thoughts on this proposed response to the charge question. Dr. Gbur stated that he agreed, because the Board has made similar recommendations in the past that were subject to EPA reconsidering or elucidating the study's assumptions.

Dr. Dawson proposed how to phrase the response to the charge question, as:

> Yes, the protocol is likely to generate scientifically reliable data that are useful for assessing exposure, subject to the caveats and limitations described below or in the HSRB report:
> - Limitations on the ability to generalize to consumers,
> - Some limitations on the ability to assess some of the covariates,
> - Recommendations about clarifying about how these covariates would be measured or documented, and
> - Along with the whole series of the Board's scientific recommendations.

Dr. Dawson asked for a show of hands through the webinar, and all Board members agreed.

Board Discussion—Ethics

Dr. Dawson asked discussant Dr. Galbraith to provide comments. Dr. Galbraith noted that Dr. Drue Barrett would also contribute to this discussion.

> **Charge to the Board - Ethics:**
> ***Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?***

Dr. Galbraith stated that the use of an Institutional Review Board (IRB), use of a surrogate product, and the exclusion of pregnant and nursing women were important for risk minimization. Because Schulman IRB is registered and a known entity, that satisfies the ethics requirements.

Dr. Galbraith stated that the surrogate product was selected based on low toxicity at commercial concentrations. He mentioned that subjects with known allergies and skin issues will be excluded. The subjects will have multiple barriers (e.g., clothing) and will bring their own respirators. The potential for heat stress was reduced by conducting the study during the winter and including SOPs in the study to reduce heat stress.

Dr. Galbraith explained how the research team will have access to emergency medical services (EMS), if needed, as well as posters and a health care person at the test site. He noted that the risks of moving paint buckets are minimal and the psychological risks (e.g., dressing and undressing) are minimal and clearly explained in the consent form. Confidentiality will be respected and compensation is not a problem. The inclusion/exclusion criteria are well defined.

Dr. Galbraith recommended removing the upper age limit (65 years old) because the eligibility criteria are designed to select physically healthy individuals. Initially, he believed that the consent form was clear, but now recommended that some language could be simplified. He stated that the bilingual issues (English and Spanish) were addressed.

The exclusion of pregnant women and children will occur through requiring a government-issued photo ID and pregnancy testing. Pregnancy testing will occur after giving consent, and will be conducted at the test site. Researchers will record the pregnancy test results, but kits will be discarded in opaque bags.

Dr. Galbraith stated that he had a few recommendations:

- Remove upper age limit;
- Add requirement to include government-issued photo ID as part of recruitment materials, because otherwise candidates might experience anxiety later if asked for ID during the consent process;
- Address concern that respirators should be mentioned in recruitment materials;
- Address concern about OSHA recommendation for two (2) forms of hearing protection;
- Clarify how the study protocol will handle a candidate that does not know their allergies; and

- Clarify about the use of snacks.

Overall, Dr. Galbraith concluded that the study is likely to meet the requirements of 40 CFR part 26, subparts K and L. Dr. Dawson mentioned it would be important to add clarification about subjects bringing respirators.

Dr. Barrett discussed some additional items. Because professional painters will identify by self-report of their professional status, Dr. Barrett stated that more discussion of whether their respirators are the appropriate type and fit properly may be needed. She suggested that the researcher's photographing and videotaping plans need clarification in the consent form. Other items that needed clarification are whether alternates may need to come to the test site on short notice, what short notice means, and if they cannot come whether such alternates will still get compensation. Dr. Barrett agreed that it was necessary to include the need for a government-issued photo ID as part of recruitment materials.

Dr. Dawson asked whether recruitment materials could mention the need to bring a respirator and also mention that the respirator will be checked to determine if it fits properly. Dr. Klimecki stated that suggestion seemed good, but emphasized his main point earlier was that researchers should not have to determine if painters are using respirators properly.

Dr. Ferguson explained some of the typical requirements for respirator use, such as training, medical exams, and monitoring for breathing trouble. Ms. Rosenheck asked how those could be implemented during the study, and whether it would be reasonable to disqualify candidates who did not have respirator training or fit testing. Ms. Rosenheck noted that disqualifying such candidates might skew subjects to large employers who have a formal safety program. Dr. Cavallari noted that the study sponsor would not be the employer, so it may be difficult to impose requirements. Mr. Dole added that he believed there was no specific OSHA requirement about using a respirator when using paint sprayers. Dr. Cavallari stated that the Safety Data Sheet (SDS) recommends respirators as a good work practice. Dr. Dawson asked whether some subjects who do not normally use a respirator on their job could be provided a respirator by the study.

Dr. Klimecki stated that although respirators were not his expertise, he could not see how subjects could be placed in indoor rooms painting without respirators. Dr. Dawson asked Board members whether subjects would need respirators, and Dr. Klimecki and Dr. Ferguson said yes.

Dr. Dawson asked whether adding a requirement that subjects needs respirators and fit testing was an unreasonable expense. Dr. Ferguson discussed how she handled respirators in her lead studies. Mr. Dole stated that wearing a filtering face piece respirator does not require a medical exam. Dr. Ferguson asked whether the study could include a 2-hour program for respirator training and fit testing. Ms. Rosenheck believed that suggestion would make the study more onerous, and added that she believed it will not be difficult to find painters who normally would wear a respirator at their job. Ms. Rosenheck added that if it was necessary to ask about respirator training and fit testing, then the study might not be able to recruit some individuals who normally wear a respirator.

Dr. Klimecki suggested that someone with occupational health credentials should be involved in making this decision. Dr. Cavallari and Mr. Dole both stated they are Certified Industrial Hygienists (CIH).

Dr. Dawson asked whether subjects would be willing to take training and get a respirator, and then Dr. Ferguson noted that respirator training programs are available in most cities.

Dr. Cavallari commented that she had reviewed the SDS again, and as a CIH, had determined it was not clear what the exposure levels would be. Dr. Cavallari stated the SDS for the paint showed that the hazardous ingredients are dust, not volatile organic compounds (VOCs). Mr. Dole pointed out that the SDS for the paint now on the Sherman Williams website was dated 2017, so it had been updated, and he read some information from it. Mr. Dole explained that the MSDS, dated June 15, 2016, included in the protocol, recommended an organic vapor/particulate respirator approved by NIOSH/MSHA [sic] for protection against materials in Section 2. [Note: NIOSH/MSHA is a typo and should be NIOSH/OSHA.] Mr. Dole explained that the materials listed in Section 2 were all particulates. Dr. Cavallari, Dr. Ferguson, and Mr. Dole discussed whether N95 respirators could be used in the study, and whether N95 respirators would require a medical exam or fit testing. Ms. Rosenheck commented that specifying a certain type of respirator and fit testing would create problems recruiting for the study.

Dr. Dawson wrapped up the discussion by stating that the Board members need to balance protection of subjects with not making studies impossible to implement. Dr. Dawson stated that the Board could coordinate by email to finalize a recommendation on the issue of subjects' respirator use within the parameters agreed to, and the Board members agreed. The HSRB's final recommendations will be presented at the next meeting on December 12, 2017.

Dr. Dawson asked Dr. Galbraith if he wanted to propose a response to the charge question, pending the resolution of the respirator question. Dr. Galbraith proposed:

> Contingent upon resolution of the respirator issue, the study is likely to meet the applicable standards of subparts K and L of 40 CFR part 26, provided that the study is modified and clarified in the ways discussed in the written comments. This would include removal of the upper age limit, mentioning the photo ID in the recruitment materials, and the list that the scientist reviewers had provided earlier.

Dr. Dawson asked for a show of hands through the webinar, and all Board members agreed.

Mr. O'Farrell asked Dr. Dawson whether the respirator question would be discussed the next day or at the next HSRB meeting. Dr. Dawson stated the respirator question will be resolved at the next meeting.

Board Discussion and Decision on July 26, 2017 Meeting Final Report

Dr. Dawson noted that the report on the mosquito repellent study, which was discussed at the July meeting, had only a minor edit and no substantive changes. The question was whether to conduct testing for multiple pathogens, which would require working through local mosquito control boards. The Board concurred with the EPA recommendation that if there was no epidemiological evidence of the risk of other diseases (e.g., Dengue), then such testing was not needed. Dr. Dawson asked for any comments, and there were none. Dr. Dawson then asked for vote to finalize the report by a show of hands through the webinar, and all Board members agreed.

Adjournment

Dr. Dawson stated that the Board had concluded the Agenda for the October meeting. Dr. Dawson stated that the Board members would have an email exchange for more information on the respirator question. Ms. Rosenheck emphasized that risks could be increased if all subjects were required to wear the same respirator, especially if it offered less protection than the respirator that subjects would normally use on their job. Ms. Rosenheck mentioned that potential for increased risk had already been discussed with EPA. Dr. Dawson stated that HSRB will consider that point because the goal is to protect subjects.

Dr. Dawson thanked the Board members for their efforts and turned the meeting over to Mr. O'Farrell. Mr. O'Farrell announced that the Agenda for the October meeting was completed, and there was no meeting the following day.

Mr. O'Farrell announced that the next HSRB meeting is scheduled for December 12, 2017. The times and agenda for this meeting will be posted on the HSRB website.

Mr. O'Farrell thanked the HSRB members for their participation and adjourned the meeting at 6:15 p.m. EDT.

Respectfully submitted:

Thomas O'Farrell , 1/19/18

Thomas O'Farrell
Designated Federal Officer
Human Studies Review Board
United States Environmental Protection Agency

Certified to be true by:

Liza Dawson, Ph.D.
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.

Attachment A
EPA HUMAN STUDIES REVIEW BOARD MEMBERS

Chair

Liza Dawson, Ph.D.
Research Ethics Team Leader
Division of AIDS
National Institute of Allergy and Infectious Diseases
National Institutes of Health
Bethesda, MD

Vice Chair

Edward Gbur, Jr., Ph.D.
Professor of Statistics
Director, Agricultural Statistics Laboratory
University of Arkansas
Fayetteville, AR

Members

Jennifer Cavallari, Sc.D., CIH
Assistant Professor
Division of Occupational and Environmental Medicine
University of Connecticut
Storrs, CT

Alesia Ferguson, Ph.D.
Associate Professor
Department of Environmental and Occupational Health
University of Arkansas
Little Rock, AR

Kyle L. Galbraith, Ph.D.
Human Subjects Protection
Carle Foundation Hospital
Urbana, IL

Walter T. Klimecki, D.V.M., Ph.D.
Associate Professor
Departments of Pharmacology and Toxicology
The University of Arizona Health Sciences
Tucson, AZ

Randy Maddalena, Ph.D.
Physical Research Scientist
Indoor Environment Group
Lawrence Berkeley National Laboratory
Berkeley, CA

Jun Zhu, Ph.D.
Professor of Statistics and of Entomology
Department of Statistics
University of Wisconsin–Madison
Madison, WI

Consultants to the Board

Drue Barrett, Ph.D.
Lead, Public Health Ethics Unit
Centers for Disease Control and Prevention
Atlanta, GA

Kendra L. Lawrence, Ph.D., BCE, PMP
Health Sciences Product Manager
U.S. Army Medical Materiel Development Activity
Fort Detrick, MD

Attachment B
***FEDERAL REGISTER* NOTICE ANNOUNCING MEETING**

ENVIRONMENTAL PROTECTION AGENCY

[FRL-9968-88-ORD]

Human Studies Review Board; Notification of Public Meetings

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice.

SUMMARY: The Environmental Protection Agency (EPA), Office of the Science Advisor announces two separate public meetings of the Human Studies Review Board (HSRB) to advise the Agency on the ethical and scientific review of research involving human subjects.

DATES: A virtual public meeting will be held on Wednesday, October 25, 2017 and Thursday, October 26, 2017, from 1:00 pm to approximately 5:00 pm Eastern Time on both dates. A separate, subsequent teleconference meeting is planned for Tuesday, December 12, 2017, from 2:00 pm to approximately 3:30 pm Eastern Time for the HSRB to finalize its Final Report of the October 25 and 26, 2017 meeting and review other possible topics.

ADDRESSES: Both of these meetings will be conducted entirely by telephone and on the Internet using Adobe Connect. For detailed access information visit the HSRB Website: http://www2.epa.gov/osa/human-studies-review-board

FOR FURTHER INFORMATION, CONTACT: Any member of the public who wishes to receive further information should contact the HSRB Designated Federal Official (DFO), Thomas O'Farrell on telephone number (202) 564-8451; fax number: (202) 564-2070; email address: ofarrell.thomas@epa.gov; or mailing address: Environmental Protection Agency, Office

of the Science Advisor, Mail code 8105R, 1200 Pennsylvania Avenue NW, Washington, DC 20460.

SUPPLEMENTARY INFORMATION:

Meeting access: These meetings will be open to the public. The full Agenda and meeting materials will be available at the HSRB Website: http://www2.epa.gov/osa/human-studies-review-board . For questions on document availability, or if you do not have access to the Internet, consult with the DFO, Thomas O'Farrell, listed under FOR FURTHER INFORMATION, CONTACT.

Special accommodations. For information on access or services for individuals with disabilities, or to request accommodation of a disability, please contact the DFO listed under FOR FURTHER INFORMATION, CONTACT at least 10 days prior to the meeting to give EPA as much time as possible to process your request.

How May I Participate in this Meeting?

The HSRB encourages the public's input. You may participate in these meetings by following the instructions in this section.

1. Oral comments. Requests to present oral comments during either meeting will be accepted up to Noon Eastern Time on Wednesday, October 18, 2017, for the October 25 and 26, 2017 meeting and up to Noon Eastern Time on Tuesday, December 5, 2017 for the December 12, 2017 meeting. To the extent that time permits, interested persons who have not pre-registered may be permitted by the HSRB Chair to present oral comments during either meeting at the designated time on the agenda. Oral comments before the HSRB are generally limited to five

minutes per individual or organization. If additional time is available, further public comments may be possible.

2. Written comments. Submit your written comments prior to the meetings. For the Board to have the best opportunity to review and consider your comments as it deliberates, you should submit your comments by Noon Eastern Time on Wednesday, October 18, 2017, for the October 25 and 26, 2017 meeting and up to Noon Eastern Time on Tuesday, December 5, 2017 for the December 12, 2017 meeting. If you submit comments after these dates, those comments will be provided to the HSRB members, but you should recognize that the HSRB members may not have adequate time to consider your comments prior to their discussion. You should submit your comments to the DFO, Thomas O'Farrell listed under FOR FURTHER INFORMATION, CONTACT. There is no limit on the length of written comments for consideration by the HSRB.

Background

The HSRB is a Federal advisory committee operating in accordance with the Federal Advisory Committee Act 5 U.S.C. App.2 § 9. The HSRB provides advice, information, and recommendations on issues related to scientific and ethical aspects of third-party human subjects research that are submitted to the Office of Pesticide Programs (OPP) to be used for regulatory purposes.

Topic for discussion. On October 25 and 26, 2017, EPA's Human Studies Review Board will finalize the draft Final Report from the July 26, 2017 meeting and consider two topics: the Antimicrobial Exposure Assessment Task Force II Airless Sprayer Study Protocol and Pinebelt Laboratory Evaluation of Bite Protection from Repellent-Impregnated Fabrics Study Protocol. The Agenda and meeting materials for this topic will be available in advance of the meeting at http://www2.epa.gov/osa/human-studies-review-board.

On December 12, 2017, the HSRB will review and finalize their draft Final Report from the October 25 and 26, 2017 meeting, in addition to other topics that may come before the Board. The HSRB may also discuss planning for future HSRB meetings. The agenda and the draft report will be available prior to the meeting at http://www2.epa.gov/osa/human-studies-review-board.

Meeting minutes and final reports. Minutes of these meetings, summarizing the matters discussed and recommendations made by the HSRB, will be released within 90 calendar days of the meeting. These minutes will be available at http://www2.epa.gov/osa/human-studies-review-board. In addition, information regarding the HSRB's Final Report, will be found at http://www2.epa.gov/osa/human-studies-review-board or from Thomas O'Farrell listed under FOR FURTHER INFORMATION, CONTACT.

Date: 09/25/17

Robert J. Kavlock, Ph.D.
EPA Science Advisor