EPA Human Studies Review Board (HSRB)

October 23, 2018 Meeting Minutes

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

Date and Time: Tuesday, October 23, 2018, 1:00 to 5:30 pm EST.

Locations: Via teleconference and webinar

Purpose: The HSRB provides advice, information and recommendations on issues related to scientific and ethical aspects of human subjects research.

Meeting was called to order at 1:00 p.m.by Tom O'Farrell, designated federal official (DFO) for the HSRB. Roll was taken and the following members and observers were present:

HSRB members	EPA staff members
Liza Dawson, Ph.D. (HSRB-Chair) Edward Gbur, Jr., Ph.D. (HSRB Vice-Chair) Jennifer Cavallari, Sc.D., CIH Alesia Ferguson, Ph.D. Kyle L. Galbraith, Ph.D. Walter T. Klimecki, D.V.M., Ph.D. AJ Allen, Ph.D., M.D. Ann Um, Ph.D. Lisa Corey, Ph.D.	Michelle Arling (OPP) Alicia Denning (OPP) Timothy Dole (OPP) Timothy Leighton (OPP) Tom O'Farrell (OSA)
Members of the public, representatives of research sponsor and research team Greg Baumann Renee Daniel (Perspective Consulting) Jonathan Cohen (ICF) Cameron Lange (Lange Research and Consulting) Brian Lange (Lange Research and Consulting) Leah Rosenheck (LR Risk Consulting) Has Shah (American Chemistry Council) Kurd Ali (EnDyna)	

Tom O'Farrell provided an introduction to the meeting and outlined the Federal Advisory Committee Act (FACA) procedures. Dr. Tom Sinks said that EPA is working on issuing a proposed rule to harmonize Subpart K with the revisions to the Common Rule. The notice of proposed rulemaking will be posted in the Federal Register very soon for a 60 day open comment period. Ms. Michelle Arling said OPP is expecting to get results from a few insect repellent studies over the new few months and the HSRB might be reviewing these studies next spring.

The Board reviewed one protocol during the session on October 23, 2018, "A Study for Measurement of Potential Dermal and Inhalation Exposure During Antimicrobial Applications Involving Immersion, Dip, and Soak" by the Antimicrobial Assessment Task Force II. The Agency's scientific review of this protocol was presented by Timothy Leighton of the EPA Office of Pesticide Programs (OPP). The study protocol examines exposure to an antimicrobial chemical being used to sanitize hard surfaces. Three applications techniques will be used: bucket, sponge, and rag; a three compartment sink; and clean out of place where equipment is dissembled and cleaned. Full-body dosimeters will be used for the study. An ammonium chloride compound, ADBAC, will be used as a surrogate for the antimicrobial. In a guinea pig study, ADBAC was applied at 8,000 ppm and no systemic toxicity effects were noticed, only irritation. EPA believes that the predicted dermal and inhalation risk will not be a concern. EPA determined that the statistical power for the sink and the clean out of place scenarios was too low. To address this, EPA recommended increasing the range of concentrations of the compound ten-fold, and presented two options. At the high end of the range (Option 1) EPA considered the maximum allowable label application rate and at the low end of the range (Option 2) EPA considered the need to still obtain detectable residues on the sampling matrices. EPA considered Option 1 to be viable if the study site selection is not an active food serving location where the items sanitized (i.e., dishware, utensils, impellers, etc.) would be immediately be put into service and if at the end of the study the items are washed with a potable water rinse. If the conditions of Option 1 cannot be met, then Option 2 is expected to still result in detectable hand residues; residues for other body parts along with inhalation exposures are expected to be minimal, even all non-detect, and the lower concentrations might add to the uncertainty. Further calculations indicated that, assuming 100% transfer to the diet, ADBAC does not trigger any dietary risk so option one is recommended. Using the K-factor, it was determined that the sample size is large enough for the study. EPA comments on previous drafts of the protocol have been addressed. In conclusion, EPA recommended increasing the range of treatment concentrations, participants should only be eligible to participate in a single scenario, and the sponsor should make exact measurements of the volumes of treatment solutions. EPA concluded that the protocol is likely to yield scientifically reliable information and achieve its objectives.

The Board then asked questions about the science presentation. Dr. Alesia Ferguson asked what type of gloves will be used in the study. Ms. Leah Rosenheck said they are some kind of chemical resistant gloves. Dr. Jennifer Cavallari asked how many times a subject would dip their hands in the solution. Mr. Timothy Leighton answered at least 5 times. Dr. Cavallari discussed the duration of exposure and whether it is believed that a maximum dermal deposition level will be reached after some time. Mr. Timothy Leighton responded that that was the correct hypothesis. Dr. Cavallari also asked about the types and amounts of dishware used. Mr. Timothy Leighton responded that it would be many sizes of dishware used. Dr. Liza Dawson said there might be a limit on how much product will get on the skin and it might affect the proportionality estimate. Mr. Jonathan Cohen said that if it was not proportional they could look at other models like quadratic models.

Ms. Michelle Arling of EPA OPP reviewed the ethical aspects of the study protocol. In Orlando, FL, 36 subjects will be recruited for the bucket & rag/sponge study, as well as the 3-compartment sink study. The COP scenario will take place in Madison, WI because that area has a high number of food-processing facilities and the study sponsors believe that there will be a sufficient cohort of qualified candidates who have experience doing COP as part of their regular employment. Advertisements describing the study will be run in English and Spanish. Subjects must be at least 18 years old, in good health, and have

experience performing a task monitored. Pregnant or nursing women, as well as children, will be excluded from participation and females will be screened for pregnancy according to the AEATF SOP. In addition, females will be asked to confirm that they're not nursing during the screening process. Candidates would also be excluded if they have any skin conditions on their hands, face, or neck that could be exacerbated by exposure to the test substance, if they have allergies or sensitivities to chemical-based cleaning or disinfecting products or to latex, if they're unwilling to be photographed or recorded and if they're an employee or a spouse of any of the entities involved in the study. Consent meetings will be held one-one-one between the volunteer and research staff member and volunteers will be given copies of the informed consent form and asked to read it. Researchers will ask questions to ensure comprehension of the materials and subjects will be required to complete the consent form and the subject qualification sheet. There is a low probability of physical risks to subjects and the protocol proposes adequate precautions to mitigate these risks. Subjects will wear two layers of clothing and goggles or safety glasses and heat stress will be managed. Compensation for the subjects is appropriate. The protocol, informed consent form, and subject qualification form, as well as all recruitment materials were reviewed and approved by the Advarra Institutional Review Board (IRB). EPA recommended the following revisions to the protocol:

- specifying the minimum amount of experience that subjects must have to qualify for this study
- adding exclusion criteria that subjects be non-smokers or willing to refrain from smoking for the duration of the test day
- including the potential for confidentiality to be breached through photos taken of the subject
- including a discussion of the label's safety warnings as part of the consent meeting
- having available at the consent meeting a list of AEATF and ACC member companies in the event a subject has a question about whether or not they're related
- clarifying that a subject withdrawing would be assisted in removing their clothing and be instructed to wash his or her hands and forearms prior to leaving the study site
- specify the circumstances under which the data from a subject who is withdrawing from the study would be included in the results

The study is applicable to the standards under 40 CFR 26, subparts K and L because this is a proposal for third-party research involving intentional exposure for human subjects to a pesticide with the intention of submitting these data to EPA under the pesticide laws. EPA's review concluded that the requirements in subpart K, specifically those related to IRB review and informed consent, have been met. The requirement to provide the protocol, information about the IRB's review, and all informed consent and recruit materials to EPA has also been met.

The Board then asked questions about the EPA's ethics review of the protocol. Dr. AJ Allen asked if the comments from EPA and the HSRB go back to Advarra and they re-review it or just incorporate the comments. Ms. Arling responded that the sponsor will work with EPA to ensure that the comments have been addressed and then it will go back to Advarra for final review.

Mr. O'Farrell said there were no comments from the public.

The HSRB's scientific review was presented by Board members Drs. Jennifer Cavallari and Lisa Corey. Dr. Cavallari said the protocol as designed will be very useful in addressing the exposure and believes will fill

an important data gap. With respect to the recommendations covered by the EPA Science Review, she and Dr. Corey were in complete agreement with all of them, especially to change the exposure concentrations to make sure there's sufficient power. Dr. Cavallari said she had some concerns that the conditions would really represent a range of occupational exposures that would be potentially experienced. Dr. Cavallari expressed doubt as to whether the surfaces and articles to be cleaned and the time spent cleaning was truly a representative of the high end of exposure. For the bucket and sponge-rag estimate, Dr. Cavallari questioned whether the survey time of twenty minutes to one hour is adequate. Dr. Corey was concerned about the precision of the analytical techniques as far as how they're controlled in the exposure scenario. Dr. Corey also said that the target analyte is a common chemical and subjects could be bringing it in to the study in some sort of personal care product.

Drs. Ann Um and Ed Gbur presented the HSRB's statistical review of the study. Dr. Gbur said the design and analysis, the statistical part analysis, are appropriate for what EPA intends to use the data. Dr. Gbur said it was good that each of the scenarios did have multiple configurations. However, Dr. Gbur was concerned that the range of exposures was not broad enough. Dr. Um said statistical procedures were good and she agreed with EPA's recommendations. Dr. Ferguson suggested measuring the height of the person or the height of the personal sampler to the sink for inhalation exposure. Dr. Allen suggested increasing the exposure time to thirty minutes to ensure adequate exposure and questioned a need to add 10 minutes to both the lower and upper time limits so it better reflects the expected exposures. Dr. Cavallari recommended that there will be an adequate number of surfaces available, so that it's realistic to clean and do the tasks over a one-hour cycle. Dr. Cavallari provided this response to the charge which was approved by the Board: the protocol of study for measurement of potential dermal and inhalation exposure during antimicrobial applications involving immersion, dip, and soak, is likely to generate scientifically reliable data and is useful for assessing the exposure of those who use products containing antimicrobial pesticides for sanitizing surfaces and equipment, providing the changes requested by EPA and the changes requested by the HSRB, specifically the water temperature change, is taken into account and implemented.

Drs. Allen and Kyle Galbraith presented the HSRB's ethics review of the study. Dr. Allen said the objectives of this study cannot be achieved via studies using in vitro or in vivo methods in animals and the study really must be conducted in humans. Dr. Allen said the risk appears similar to those that the subjects would experience on a daily basis in the workplace and the compensation for subjects is appropriate. Dr. Allen said there were a number of recommendations made regarding ethics and privacy concerns, and recommendations in the EPA report and he agrees with all of them. Dr. Galbraith appreciated that as part of the screening process, subjects are asked specifically if they are nursing or lactating, and that this status is also an exclusion criterion. Dr. Galbraith commented favorably on the protocol provisions for recruitment is both in English and Spanish, and to have a member of the research team on site who is bilingual and who will be able to communicate with Spanish-speaking subjects at all times. Dr. Cavallari asked should the Board recommend in the study materials to explicitly tell workers who may be signing up for the process either during the recruitment or the consent phase that they will be asked not to wear gloves? Ms. Arling said it is very reasonable to add an explicit statement to the consent material stating that one of the criterion is being willing to participate without wearing gloves. The Board voted unanimously that with the recommended changes from EPA and the HSRB, that the research is likely to meet the applicable requirements of 40 CFR, part 26, sub-parts K and L.

This concluded the Board's session for October 23, 2018 and the meeting was adjourned.

Respectfully submitted:

Thomas J. O'Farrell, 2/25/19

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

Certified to be true by:

DAWSON.LIZA.1551768917 Digitally signed by DAWSON.LIZA.1551768917 Date: 2019.02.25 09:51:15 -05'00'

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 Built Environment
North Carolina A&T University
Greensboro, NC

Kyle L. Galbraith, Ph.D.
Patient Representative Coordinator
Piedmont Athens regional Medical Center
Athens, GA

Lisa Corey, Ph.D.
Toxicologist
Intertox, Inc.
Seattle, WA

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

Albert J. Allen, M.D., Ph.D.
Senior Medical Fellow
Eli Lilly
Indianapolis, IN

Eun Um, Ed.D.,
President and CEO
AMSTAT Consulting
Bethesda, MD

Lindsay McNair, M.D., Ph.D.
Chief Medical Officer
WIRB-Copernicus
Princeton, NJ

Consultants to the Board

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

Attachment B
Federal Registers Notice Announcing Meetings

ENVIRONMENTAL PROTECTION AGENCY

[FRL-9984-60-ORD]

Human Studies Review Board; Notification of Public Meetings

AGENCY: Environmental Protection Agency.

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 Tuesday, October 23, 2018, from 1:00 pm to approximately 5:30 pm Eastern Time. A separate, subsequent teleconference meeting is planned for Thursday, December 13th, 2018, from 2:00 pm to approximately 3:30 pm Eastern Time for the HSRB to finalize its Report of the October 23, 2018 meeting and review other possible topics.

ADDRESSES: All 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. To pre-register to make oral comments, please contact the DFO, Thomas O'Farrell, listed under FOR FURTHER INFORMATION, CONTACT. Requests to present oral comments during the meeting will be accepted up to Noon Eastern Time on Tuesday, October 16, 2018, for the October 23, 2018 meeting and up to Noon Eastern Time on Thursday,

December 6, 2018 for the December 13, 2018 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 via email or Fax by Noon Eastern Time on Tuesday, October 16, 2018, for the October 23, 2018 meeting and by Noon Eastern Time on Thursday, December 6, 2018 for the December 13, 2018 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 23, 2018, the Human Studies Review Board will consider a protocol titled "A Study for Measurement of Potential Dermal and Inhalation Exposure During Antimicrobial Applications Involving Immersion, Dip, and Soak" submitted by the Antimicrobial Exposure Assessment Task Force.

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 13, 2018, the HSRB will review and finalize their draft Final Report from the October 23, 2018 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: _____

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Jennifer Orme-Zavaleta, Ph.D.
EPA Science Advisor