EPA Human Studies Review Board (HSRB)

April 24, 2019 Meeting Minutes

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

Date and Time: Tuesday, April 24, 2019, 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
Jennifer Cavallari, Sc.D., (Chair) Alesia Ferguson, Ph.D. Kyle L. Galbraith, Ph.D. Walter T. Klimecki, D.V.M., Ph.D. (Vice-Chair) AJ Allen, Ph.D., M.D. Ann Um, Ed.D. Lisa Corey, Ph.D. Randy Maddalena, Ph.D. Lindsay McNair, M.D.	Michelle Arling (EPA, OPP) Matthew Crowley (EPA, OPP) Tom O'Farrell (OSA)
Members of the public, representatives of research sponsor and research team Mike Krolski (Bayer CropScience) Dave Barnekow (AHETF) Dave Baughger (EXP Corporation) Dave Johnson (Johnson Management and Consulting) Larry Holden (AHETF) Adam Allington (Bloomberg) Benson Leopold (AHETF) Eric Bruce (AHETF) Jeff Holmsen (AHETF) Ed Scollon (Valent USA) Steve McEuen Jason Johnston Kurd Ali (EnDyna)	

Tom O'Farrell provided an introduction to the meeting and outlined the Federal Advisory Committee Act (FACA) procedures and took role of the meeting participants.

The Board reviewed one study during the session on April 24, 2019, "Dermal and Inhalation Exposure to Workers during Mixing, Loading and Application of Pesticides in Managed Horticultural Facilities using Powered Handgun Equipment" by the Agricultural Handler Exposure Task Force (AHETF).

The Agency's scientific review of this protocol was presented by Matthew Crowley of the EPA Office of Pesticide Programs (OPP). The purpose of the study was to capture the range of expected dermal and inhalation exposures for workers mixing/loading and applying (M/L/A) pesticides using powered handgun in equipment in facilities such as greenhouses and nurseries. The protocol was originally reviewed by the HSRB in 2012 and amendments were made to increase the potential for successful recruitment and to update analytical methods. EPA accepted those amendments. There were deviations from the protocol regarding exposure monitoring and analytical methods but EPA determined that those did not compromise the exposure results. To address recruitment difficulties, the protocol was amended to expand monitoring areas and allow monitoring of more than 3 workers per area. The exposure analysis used exposure normalized by the amount of active ingredient using empirical estimates, simple random sample, and mixed models. EPA concluded that data can be used for federal pesticide registration as it represents compliance with product labels and other federal regulatory requirements, reasonably represents the expected range of exposures for this scenario and will be used to quantify occupational exposure for pesticides with this specific use pattern. Because the accuracy criteria were not met, EPA will consider incorporating an adjustment/multiplier to the exposure values. EPA considered but decided against requiring the inclusion of workers who mix wettable powder pesticide formulations. As a result, the study only included monitoring of workers who mixed liquid concentrates and dry flowables (i.e., water-dispersible granules).
This will require further internal EPA discussion regarding comparison of available mixer/loader data (dry flowables vs. wettable powders), mixing/loading versus application, and review of previously "rejected" data. Participants that conducted overhead spraying (7 of 27 workers) wore chemical-resistant hats as required by the protocol. However, the results presented in the AHETF submission and EPA review are all exposures assuming no chemical-resistant hats were worn. This will require further review by EPA. In conclusion, EPA found that the study design was acceptable, with the diversity of conditions adequately captured, monitoring methods consistent with EPA guidelines and prevailing research, and acceptable AHETF analysis of primary and secondary objectives, and is superior to existing data.

The Board then asked questions about the science presentation. Dr. Alesia Ferguson had several comments that were discussed:

- Were any residue on the chemical resistant hat measured and combined with inner and outer patch for dermal exposure? Ideally the outer patch would have collected all residues.
- If subjects are lifting/pulling anything, moderate activity can be assumed also and a higher inhalation rate can be used?

- If some labels do not require the use of chemical-resistant gloves, dermal exposure estimates should account for this? Meaning should some of the ME's have included hands without gloves.
- If a non-linear relationship between active amount of an active ingredient and total exposure was not determined, how will EPA use this information to extrapolate? If the data was modeled separately as those who used the hand wand versus the hand gun, do we obtain an improved linear relationship?
- Where the deviations in protocol not discovered in time to replace the 3 ME's?
- Although this is not the way EPA wishes to use the information, is there a relationship between exposure time and amount of solution sprayed or exposure time and the dermal or inhalation measurements. There was a high variability in activities, including the exposure time.
- Dr. Maddalena noted that for MU3 analytical chemistry results, the value was way above the dynamic range and was concerned that they may have missed the highest exposed individual as this individual was excluded from the analysis. AHETF member clarified that they could not reanalyze this sample because the lab was not capable of analysis, Furthermore the inhalation results were lost due to pump failure. Therefore MU03 had incomplete dosimetry and was excluded.Dr. Lisa Corey asked a question about the incorporation of the qualitative data into the analysis. Matt Crowley responded that the data remains qualitative, yet they have the ability to tabulate it.
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Ms. Michelle Arling of EPA OPP reviewed the ethical aspects of the study protocol. The HSRB recommended minor revisions when they reviewed the protocol in 2012, which the AHETF addressed prior to the study. EPA's ethics review compared the recruitment approach used in the study with the process identified in the protocol and SOPs. It was determined that AHETF generally followed the recruitment outlined in the protocol & SOPs with amendments approved by the overseeing IRB. All subjects met eligibility criteria listed in SOP-11.B. and additional criteria specified in the protocol. Participating subjects completed the informed consent process described in the protocol and consent occurred after recruitment and prior to monitoring. Subjects were informed of the pesticide active ingredient and end-use product before the monitoring event began and it was noted on the consent form. Subjects wore required personal protective equipment and outer clothing according to the protocol. A medical professional was present and monitored the health of the subjects. Protocols related to managing heat stress were followed. The protocol was amended 9 times after it was signed, and all amendments were approved by the IRB. Three IRBs had oversight, due to consolidation within the industry – there was continuous oversight of the study by IRBs familiar with the research. The study was overseen by Independent Investigational Review Board, Schulman and Advarra. All subjects were over 18 years old and not pregnant. The protocol was implemented as approved and amended, and subjects were fully informed, and their consent was voluntary. In conclusion, the information indicates that Study AHE600 was conducted in substantial compliance with subparts K and L of 40 CFR part 26.

There were no questions about the Ethics Review from the HSRB.

Tom O'Farrell announced there were no comments from the public.

The HSRB's scientific review was presented by Board members Drs. Randy Maddalena and Alesia Ferguson. Issues were discussed concerning measuring residues on the chemical resistant hat, activity level and inhalation rate, and if some labels do not require the use of chemical-resistant gloves, whether dermal exposure estimates should account for this. Dr. Ferguson noted that the dermal exposures presented are reflective of people wearing chemical resistant glove.

The Board made the following recommendations for EPA for the use of data:

- account for exposure residues on protective hats; there is a concern that the exposure may be underestimated
- consider using moderate activity levels and higher inhalation rates for calculating inhalation exposures
- extrapolate hand exposure to hands when no gloves are used.
- analyze relationships between dermal exposure and AaiH separately for workers who used the hand wand vs. hand gun
- evaluate relationship between exposure time and amount of solution sprayed or exposure time and the dermal or inhalation measurements.

The Board's statistical review was given by Dr. Ann Um. It was determined that the results are consistent with a study design of at least 80% power and that the statistical procedures were appropriate. The HSRB supports using the adjustment/multiplier that was recommended by EPA to account for the less than desired accuracy of the study.

The Board decided unanimously that the research presented in AHE600 and the associated documents is scientifically sound, providing reliable data useful for assessing the exposure of those who manually open, pour and mix pesticide products in spray solution tanks and apply the solutions using powered handgun equipment in managed horticultural facilities such as greenhouses and nurseries.

Drs. Lindsay McNair and Kyle Galbraith presented the HSRB's ethics review of the study. Drs. McNair and Galbraith agreed with the EPA findings and conclusions regarding the ethical considerations of the study. The Board voted unanimously that the study was conducted in substantial compliance with the applicable requirements of 40 CFR, part 26.

This concluded the Board's session for April 24, 2019 and the meeting was adjourned.

Respectfully submitted:

Thomas O'Farrell, 7/18/19

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

Certified to be true by:

Jennifer Cavallari, Sc.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

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

Vice Chair

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

Members

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

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

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

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-9991-24-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 Wednesday, April 24, 2019, from 1:00 pm to approximately 5:30 pm Eastern Time. A separate, subsequent teleconference meeting is planned for Tuesday, June 11th, 2019, from 2:00 pm to approximately 3:30 pm Eastern Time for the HSRB to finalize its Report of the April 24, 2019 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 Wednesday, April 17, 2019, for the April 24, 2019 meeting and up to Noon Eastern Time on Tuesday, June 4, 2019 for the June 11, 2019 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 Wednesday, April 17, 2019, for the April 24, 2019 meeting and by Noon Eastern Time on Tuesday, June 4, 2019 for the June 11, 2019 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 April 24, 2019, the Human Studies Review Board will consider a study submitted by the Agricultural Handlers Exposure Task Force (AHETF) titled "Determination of

Dermal and Inhalation Exposure to Workers during Mixing, Loading and Application of Pesticides in Managed Horticultural Facilities using Powered Handgun Equipment".

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 June 11, 2019, the HSRB will review and finalize their draft Final Report from the April 24, 2019 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