Summary Certification

I, Julia Sharp, Co-Chair of the Human Studies Review Board, certify that the meeting minutes for the date of __May 1, 2025___, as hereby detailed, contain a record of the persons present and give an accurate description of matters discussed and conclusions reached and copies of all reports received, issued or approved by the advisory committees. My signature date complies with the 90-day due date after each meeting required by the GSA Final Rule.

Julia L. Sharp Digitally signed by Julia L. Sharp
Date: 2025.05.21 10:07:35 -06'00'

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Julia Sharp, HSRB Co-Chair

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Date

EPA Human Studies Review Board (HSRB)
May 1, 2025 Meeting Minutes

Committee Members: See Appendix A: HSRB Current Committee Membership.
Date and Time: Thursday May 1, 2025, 1:00 to 2:00 p.m. ET
Location: Via Zoom
Purpose: The HSRB provides advice, information, and recommendations on issues related to scientific and ethical aspects of human subject research.
HSRB Website: https://www.epa.gov/osa/human-studies-review-board

Table of Contents

Thursday, May 1, 2025

A. Meeting Topics and Charge Questions

Topic: "Evaluation of Topically Applied Insect Repellent Products Containing Oil of Lemon Eucalyptus (Citriodiol) Against Mosquitoes in the Field." March 22, 2024. Sponsored by Citrefine International Ltd. Moorfield Rd. Yeadon, Leeds. LS19 7BN U.K. MRID 523504. Protocol version 0.1 as amended March 11, 2024. IRB approved March 7, 2024. 117 p.

Charge to the Board – Science: Is the protocol "*Evaluation of Topically Applied Insect Repellent Products Containing Oil of Lemon Eucalyptus (Citriodiol) Against Mosquitoes in the Field*" likely to generate scientifically reliable data, useful for estimating the amount of time each of the products tested repels mosquitoes?

Charge to the Board – Ethics: If amended to address the EPA's and the HSRB's recommendations, is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

B. Convene Meeting and Introduction of Members

Emily Sokol, Designated Federal Official (DFO), EPA HSRB, Office of Science Advisor, Policy, and Engagement (OSAPE)

Ms. Emily Sokol, the DFO for HSRB, called the meeting to order at 1:00 p.m. ET. Ms. Sokol introduced the meeting and outlined the Federal Advisory Committee Act procedures. Dr. Julia Sharp, HSRB Co-Chair, performed a roll call of meeting participants. The following members and observers were present:

HSRB members
Julia Sharp, Ph.D., Co-Chair (National Institute of Standards and Technology) Albert J. Allen, M.D., Ph.D. (Consulting Specialist) Gretchen Bruce, DABT (Intertox, Inc.) Nicole Deming, J.D., M.A. (Case Western Reserve University, School of Medicine) Richard Feinn, Ph.D., M.A. (Qinnipiac University) Thomas Gillam-Shaffer, MPH (Michigan Public Health Institute/State of Michigan Partnership) Weiying Jiang, Ph.D. (California Environmental Protection Agency) Srikumaran Melethil, Ph.D., J.D. (University of Missouri-Kansas City) George Milliken, Ph.D. (Milliken Associates, Inc.) Sinziana Seicean-Boose, M.D., Ph.D., M.P.H., LLC (Case Western Reserve University) Joseph Tuminello, Ph.D. (McNeese State University)
EPA staff members
Emily Sokol (EPA, OSAPE) Michelle Arling (EPA, Office of Pesticide Programs [OPP]) Stephanie Cooke (EPA, Program in Human Research Ethics and Oversight [PHERO]) James Nguyen (EPA, OPP) Shweta Sharma (EPA, OPP)

Mira Schwadron (EPA, Oak Ridge Associated Universities) Monique Tadeo (EPA, PHREO) Philip Villanueva (EPA, OPP)
Members of the public, representatives of research sponsor, and research team
Sarah Dewhirst (ARTEC) Afroditi Katsigiannakis (ICF, Contractor Support) Emily Pak (ICF, Contractor Support) Julie Palm (SC Johnson) Daniel Usry (SC Johnson) Angelina Winnett (ICF, Contractor Support)

C. Meeting Administrative Procedures

Emily Sokol, DFO, EPA HSRB, OSAPE

Ms. Sokol reviewed the Zoom platform tools and features and stated that the purpose of the meeting was to review and discuss the HSRB report on the paper sponsored by Citrefine International Ltd., (2024) "*Evaluation of Topically Applied Insect Repellent Products Containing Oil of Lemon Eucalyptus (Citriodiol) Against Mosquitoes in the Field*." Ms. Sokol noted that the minutes of the meeting and a report will be prepared, certified, and posted on the website within 90 days of May 1, 2025.

D. Introduction of EPA Staff

Michelle Arling, J.D., OPP

Ms. Michelle Arling introduced herself and the members of the EPA OPP staff to the Board.

E. Opening Remarks and Meeting Process

Julia Sharp, Ph.D., HSRB Co-Chair

Dr. Sharp welcomed the Board and reviewed the meeting's logistical procedures.

F. Updates from EPA HSRB Review Official

Monique E. Tadeo, Human Subjects Research Review Official, PHREO

Ms. Monique Tadeo introduced herself to the Board and shared that the Department of Health and Human Services' Secretary Advisory Committee for Human Research Protection has been disbanded.

G. Updates from OPP

Michelle Arling, J.D., OPP

Ms. Arling shared the EPA plans for the HSRB to review a protocol for an occupational worker exposure study in the Fall.

H. Public Comment

There were no public comments.

I. Review and Finalize HSRB Report

Julia Sharp, Ph.D., HSRB Co-Chair

Dr. Sharp reviewed and discussed comments in the draft HSRB report with the Board.

- **Julia Sharp:** The EPA has requested the report language be changed to "subjects will be needed for each field test day." in the science review portion of the report. Is everyone okay with this change?
    - **Weiying Jiang:** I am okay with that change.
    - **Gretchen Bruce:** I am as well.
    - **Richard Feinn:** Me too.
- **Julia Sharp:** The EPA added a few other minor comments. Does anyone have concerns with these edits?
    - No concerns were raised.
- **Julia Sharp:** There were revisions made to the statistical analysis portion of the report to increase clarity of the sample size estimate and required level of precision.
    - **Richard Feinn:** I think the text is better now.
    - **George Milliken:** No comments from me.
- **Julia Sharp:** I noticed that Dave had a comment about page 28 of the EPA's review, which states there are two alternates. I have added a recommendation to the report to change this number to five. Thank you for noting that, Dave.
- **Julia Sharp:** George, would you like to speak to your comment about time to landing time interval?
    - **George Milliken:** There was concern of bias regarding the time interval, since mosquito landing can occur at any time between two measured time periods. The landing time will likely be plus or minus 15 minutes. I think this is reasonable and I do not see a concern with this measurement.
    - **Julia Sharp:** Do you want to add anything to the comment?
    - **George Milliken:** I do not think there is a concern for bias because it is so small compared to the measurement. I would delete the comment.
    - **Julia Sharp:** Weiying and Gretchen, do you have any concerns with removing the comment?
    - **Gretchen Bruce**: What was the recommendation?
    - **Julia Sharp**: George recommends the removal of the time to landing comment and associated recommendation.
    - **Gretchen Bruce**: There could be left censoring. If you are saying there is no real bias, then I am okay with removing it.
    - **George Milliken**: The 15-minute bias is small compared to the target value,

which is likely 4-6 hours.

- **Weiying Jiang**: My understanding is that this information is used to support label registration for the product, which is often in hour units. This is within the uncertainty and standard deviation, and I am okay with this.
- **Gretchen Bruce**: Considering that perspective, I am okay with removing the comment.
- **Julia Sharp**: Weiying, are you okay with removing the comment and recommendation?
- **Weiying Jiang**: Yes.
- **Julia Sharp**: Rich, are you also okay with removing the comment and recommendation?
- **Richard Feinn**: If the time of exposure changed from 5 minutes to 1 minute, would there be a difference? It seems that the study design assumes that if there is any risk of mosquito landing, it will happen during the exposure period. However, a mosquito could not be around during that short interval and thus a landing could be missed.
- **George Milliken**: Are you concerned that the 5-minute interval is not long enough?
- **Richard Feinn**: If study participants are at risk for the entire 30 minutes, there may have been a portion of that time where a mosquito is nearby and lands. However, landing may not happen continuously for 30 minutes so a landing may be missed when observing only the first 5-minute exposure period. What is the necessity of the 25-minute break that they cannot be at risk?
- **Julia Sharp**: Shweta, can you weigh in here?
- **Shweta Sharma**: I discussed this with the EPA's statisticians and have some idea. Phil or James, please weigh in.
- **James Nguyen**: This is how the study was designed. The mosquito landing is assessed for 5 minutes every 30 minutes so that is the interval censor. There is a Kaplan-Meier analysis that ensures that there is no bias in the results. The EPA currently uses the right censor analysis. An interval censor analysis can be conducted, and I do not believe bias is an issue.
- **Richard Feinn**: This is different than outcomes (e.g., cancer or death). At a certain timepoint someone may develop cancer, and that will not be missed. However, a mosquito could land in 15 minutes, and it could be missed.
- **Julia Sharp**: I think this has to do with the study site, participant engagement, and mosquito population. Can the EPA answer whether there is a chance that a mosquito landing is missed?
- **Michelle Arling**: Are you asking about during the 5 minutes where the participants are exposed?
- **Julia Sharp**: I think so.

- **Michelle Arling**: The protocol ensures that only a limited amount of skin is exposed, and participants are trained in advance to observe mosquito behavior during the 5-minute exposure period. Additionally, participants are paired so there are two individuals always observing. In that 5-minute interval, it is possible to miss a mosquito landing, but the points mentioned previously reduce that chance. Continuous monitoring may have a higher risk of missing a landing, because it is difficult to pay attention for an extended period of time.
- **George Milliken**: I agree with that.
- **Richard Feinn**: I do not think a mosquito landing will be missed in the 5-minute exposure period, but it may be missed in the following 25-minute interval. In real world product use, an individual would be outside for an entire 30 minutes. A mosquito may land on someone at the 15-minute mark; however, this would be missed in the current study design.
- **George Milliken**: We are assuming that the mosquitoes will land occasionally. I think 5 minutes is a good interval. It will be difficult to concentrate for all 30 minutes. Theoretically, observing for the entire time would provide better data, but practically, it will likely lead to missed landings.
- **Philip Villanueva**: There is a control group to ensure mosquitoes are landing within that 5-minute period within that study site's area. Once mosquitoes start feasting, they go towards any available subject. It is assumed that if a landing does not occur on treated subjects within the first 5 minutes, then a landing is unlikely to occur at all, since there is evidence that landings are occurring on untreated subjects.
- **James Nguyen**: I understand your concern, however this does not impact the analysis. An interval analysis can be conducted.
- **George Milliken**: Left censoring is interesting, but it is unknown which mosquitos are left censored. It is known that left censoring is possible, but the data are unknown.
- **Richard Feinn**: This discussion was helpful and convincing. I now believe if a mosquito landing occurs, it will happen during the first 5-minute interval.
- **Julia Sharp**: Thank you, I will remove the comment and recommendation.

Dr. Sharp thanked the Board for the discussion and requested that Dr. Gretchen Bruce address the comment regarding special independence on page 11 of the final *Report of the U.S. Environmental Protection Agency Human Subjects Review Board*. The comment concerns the 3-meter distance between sampling stations and whether this is sufficient to prevent diffusion. Dr. Bruce brought up the World Health Organization (WHO) standard of 20 meters distance, and inquired how the recommendation should be worded to request evidence supporting the 3-meter distance. Dr. Sharp clarified that the HSRB provides recommendations only, and that the authors are not bound to provide evidence. Alternatively, Dr. Sharp highlighted that the HSRB can give recommendations addressing a scenario where authors cannot provide evidence.

- **George Milliken:** I would like to point out that mosquitoes can fly a large distance quickly, as I have seen in some infestations that I have been involved with. If the mosquito population is pretty dense, then I do not think this is a problem. If they are more sparsely distributed, this sampling distance could be an issue.
- **Julia Sharp:** EPA staff members, do you have a comment about whether you could provide evidence or a reference to the use of the 3 meters?
    - **Michelle Arling:** I think what would happen is we would request this from the study sponsor. So, the EPA would not find the evidence, but we would pass the recommendation along.
    - **Julia Sharp:** Shweta, did you want to follow up on that?
    - **Shweta Sharma:** I wanted to mention that 3 meters is our recommendation in the product performance guidelines. They are following the guidance, and we do not follow the WHO guidance of 20 meters.
    - **George Milliken:** This study has nine stations so if you have [them] 20 meters apart, that is a very large area that would be difficult to handle.
    - **Gretchen Bruce:** Do we want to keep that recommendation then, if it is part of the guidelines?
    - **Julia Sharp:** We could change the recommendation to provide a reference for the 3 meters.
    - **George Milliken:** 20 meters with nine stations is 180 meters, two football fields, which would be difficult to carry out the study on.
    - **Julia Sharp:** What guideline was the 3 meters from?
    - **Shweta Sharma:** The Product Performance Guidelines.

Dr. Sharp asked if all Board members agreed on updating the text in the HSRB report with the new language regarding 3 meters and a citation. The HSRB members verbally gave their approval to the updated language. Dr. Sharp then transitioned to reviewing other changes, including a comment on subject alternates on page 11 of the final report and smaller language changes such as adding "up to" for the number of subjects enrolled. Dr. Sharp requested Ms. Nicole Deming's approval, which Ms. Deming provided.

- **George Milliken:** I have a question regarding positive controls on page 8. We are not trying to compare different products and instead find out how long this product is working. We use the non-positive controls to ensure a sufficient population of mosquitoes are in the area and then see how long this particular product lasts. And so, we do not need to know if this product lasts longer than some other product or not. Because this is a comparative study not an estimative study, we do not need positive controls in the way things are written, and I suggest removing this comment.
    - **Weiying Jiang:** Yes, I raised this point because positive controls were mentioned in the published EPA Guidance. The EPA staff members mentioned at the last meeting that they are in the process of updating this Guidance and so I am

comfortable removing this language. Can anyone from the EPA confirm this?

- **Shweta Sharma:** Yes, I mentioned in the general meeting that we no longer recommend adding positive controls.
- **Julia Sharp:** Gretchen, is it okay with you to remove this?
- **Gretchen Bruce:** Yes, that is alright.

Dr. Sharp asked if there were any objections from the HSRB and, hearing none, asked if there were any additional comments, questions, or changes to the report. The Board did not have additional changes.

Dr. Sharp then summarized the next steps in the process, which are to approve the report with the agreed changes, to technically edit the report by the contractor, and finally to publish the report on the HSRB website. She then asked the HSRB for final approval of the updated report through a roll-call vote. The HSRB members attending the meeting unanimously approved the updated report. Dr. Sharp thanked the HSRB and confirmed that the changes to the report will be made.

J. Adjournment

Ms. Sokol thanked the HSRB, and the meeting concluded.

The meeting adjourned at 1:57 p.m. ET.

Attachment A: HSRB Current Committee Membership

Name	Title	Affiliation
Julia Sharp, Ph.D.	Mathematical Statistician	National Institute of Standards and Technology Fort Collins, CO
Philip Day, Ph.D.	Assistant Professor	University of Massachusetts, Chan Medical School Worcester, MA
Albert J. Allen, M.D., Ph.D.	Consulting Specialist	Self-employed
Gretchen Bruce, DABT	Director of Toxicology	Intertox, Inc.
Chad Cross, Ph.D., MFT, PStat®	Professor, Faculty in Residence	University of Nevada Las Vegas, NV
Nicole Deming, J.D., M.A.	Assistant Dean, Faculty Affairs and Human Resources	Case Western Reserve University, School of Medicine Cleveland, OH
Richard Feinn, Ph.D., M.A.	Professor of Basic Sciences, Chairperson of University IRB	Quinnipiac University
Thomas Gillam-Shaffer, MPH	Environmental Health Navigator; Adjunct Professor of Public Health	Michigan Public Health Institute/State of Michigan Partnership
Weiying Jiang, Ph.D.	Staff Toxicologist	California Environmental Protection Agency Sacramento, CA
Thomas Lewandowski, Ph.D.	Principal	Gradient Seattle, WA
Srikumaran Melethil, Ph.D., J.D.	Professor Emeritus	University of Missouri-Kansas City Kansas City, MO
George Milliken, Ph.D.	President	Milliken Consultants Manhattan, KS
Sinziana Seicean-Boose, M.D., Ph.D., M.P.H., LLC	Assistant Professor	Case Western Reserve University Cleveland, OH
Joseph Tuminello, Ph.D.	Assistant Professor	McNeese State University Lake Charles, LA
David Williams, Ph.D.	Distinguished	Oregon State University

	Professor	Corvallis, OR

Attachment B: Federal Register Notice Announcing Meetings

ENVIRONMENTAL PROTECTION AGENCY

[FRL-12412-01-ORD]

Human Studies Review Board Meetings—2025

AGENCY: Environmental Protection Agency

ACTION: Notice of public meeting

SUMMARY: The Environmental Protection Agency (EPA), Office of Research and Development (ORD), gives notice of its public meetings of the Human Studies Review Board (HSRB) for 2025. 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.

DATES: Three three-day virtual public meetings will be held on:

1. April 3–4, 2025
2. July 22–24, 2025
3. October 14–16, 2025

Meetings will be held each day from 1 p.m. to 5 p.m. Eastern Time. For each meeting, separate follow-up meetings are planned for the HSRB to finalize reports from the three-day meetings. These follow-up meetings will be held from 1 p.m. to 5 p.m. Eastern Time on the following dates: May 1, 2025; August 26, 2025; and November 18, 2025.

ADDRESSES: All of the meetings are open to the public and will be conducted entirely virtually and by telephone. For detailed access information and meeting materials please visit the HSRB website: *https://www.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), Emily Sokol, via phone/voicemail at: 202-564-1451; or via email at: *sokol.emily@epa.gov*.

SUPPLEMENTARY INFORMATION:

Background

The HSRB is a Federal advisory committee operating in accordance with the Federal Advisory Committee Act 5 U.S.C. 10. The HSRB provides advice, information, and recommendations on issues related to scientific and ethical aspects of proposed or completed human research submitted by EPA, including research involving intentional exposure of human subjects to any substance to be considered by EPA in connection with an action under FIFRA (7 U.S.C. 136-136y) or section 408 of FFDCA (21 U.S.C. 346a), and research involving intentional exposure of human subjects to pesticides to be considered by EPA in connection with an action under any statute or regulation administered by EPA.

Meeting access: These meetings will be open to the public. The full agenda with access information and meeting materials will be available prior to the start of each meeting at the HSRB website: *https://www.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, Emily Sokol 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 ten days prior to each meeting to give EPA as much time as possible to process your request.

Public Participation

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, Emily Sokol, listed under **FOR FURTHER INFORMATION CONTACT** . Requests to present oral comments during the meetings will be accepted up to noon Eastern Time, seven calendar days prior to each meeting date. 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 the meetings 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.* For the Board to have the best opportunity to review and consider your comments as it deliberates, you should submit your comments prior to the meetings via email by noon Eastern Time, seven calendar days prior to each meeting date. 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, Emily Sokol, listed under **FOR FURTHER INFORMATION CONTACT** . There is no limit on the length of written comments for consideration by the HSRB.

Topics for discussion. The agenda and meeting materials will be available seven calendar days in advance of each meeting at https://www.epa.gov/osa/human-studies-review-board.

Meeting minutes and final reports. Minutes of these meetings, summarizing the topics discussed and recommendations made by the HSRB, will be released within 90 calendar days of each meeting. These minutes will be available at https://www.epa.gov/osa/human-studies-review-board. In addition, information regarding the HSRB's Final Reports, will be found at https://www.epa.gov/osa/human-studies-review-board, or can be requested from Emily Sokol listed under **FOR FURTHER INFORMATION CONTACT**.

Dated: Kathleen Deener, Director, Office of Science Advisor, Policy, and Engagement.