



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C., 20460

OFFICE OF CHEMICAL
SAFETY AND POLLUTION
PREVENTION

April 4, 2018

MEMORANDUM

SUBJECT: Materials for Review by Human Studies Review
Board for the April 24-26, 2018 Meeting

TO: Thomas O'Farrell
Designated Federal Official
Human Studies Review Board
Office of Science Advisor

FROM: Michelle Arling
Human Research Ethics Review Officer
Office of the Director
Office of Pesticide Programs

This memorandum identifies the materials that the Environmental Protection Agency's (EPA's) Office of Pesticide Programs is providing for review by the Human Studies Review Board (HSRB or Board) at the teleconference and virtual meeting scheduled for April 24-26, 2018. During the October discussion, EPA will ask the Board to respond to specific science and ethics questions focused on the research identified below.

1. A protocol for laboratory-based testing of a tick repellent containing Oil of Lemon Eucalyptus (OLE), submitted arctec (Arthropod Control Product Centre) and by sponsored by Citrefine International.
2. A completed study submitted by the Antimicrobial Exposure Assessment Task Force II (AEATF): "Determination of Removal Efficiency of 1,2-Benzisothiazol-3(2H)-one (BIT) from Hand Surfaces Using an Isopropyl Alcohol/Water Wipe and Wash Procedure" (AEA08)
3. A completed study submitted by the AEATF: "A Study for Measurement of Potential Dermal and Inhalation Exposure During Application of a Latex Paint Containing an Antimicrobial Pesticide Product Using a Brush and Roller for Indoor Surface Painting" (AEA09)
4. A published article titled: "Assessing key safety concerns of a Wolbachia-based strategy to control dengue transmission by Aedes mosquitoes", authored by Jean Popovici, Luciano A Moriera, Anne Poinignon, Inaki Iturbe-Ormaetxe, Darlene McNaughton, and Scott O'Neill

1) Protocol: “A single group trial to determine the complete protection time of an insect repellent formulation containing 30% Citriodiol® (Oil of Lemon Eucalyptus) against three species of ticks.”

EPA has reviewed the aforementioned protocol for laboratory testing to evaluate a repellent containing 30% Oil of Lemon Eucalyptus (OLE) against three species of ticks. The protocol also includes a dosimetry phase to determine a “typical consumer dose” of the product, which will be used as the dose for the repellent testing. The EPA review evaluates the scientific aspects of the proposed research for an efficacy study to assess complete protection time of the skin-applied repellent against OPP’s guidelines (OSCPP 810.3700) and against previous recommendations from the HSRB. Ethical aspects of the proposed research are assessed in terms of the standards defined by 40 CFR 26 subparts K and L. The data collected in the study will be used to support product registration. The research has societal value because people are at risk of contracting tick-borne diseases, and the data supporting currently registered skin-applied repellents do not show the efficacy of this product.

The charge questions for the HSRB’s consideration are provided below:

Charge to the Board - Science:

- Is the protocol “A single group trial to determine the complete protection time of an insect repellent formulation containing 30% Citriodiol® (Oil of Lemon Eucalyptus) against three species of ticks” likely to generate scientifically reliable data, useful for estimating the amount of time the product tested repels ticks?

Charge to the Board - Ethics:

- Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

Documents: EPA is providing for HSRB review the following documents:

- a) Science and Ethics Review of a Protocol for Laboratory Evaluation of Skin-Applied Tick Repellent Product Containing OLE
- b) IRB-approved protocol dated July 21, 2017
- c) arctec OLE additional materials (questionnaire, advertisement, recruitment email)
- d) arctec OLE IRB correspondence and approval
- e) EPA’s comments on IRB-approved protocol
- f) EPA’s comments on IRB-approved consent

2) A completed study submitted by the Antimicrobial Exposure Assessment Task Force II (AEATF): “Determination of Removal Efficiency of 1,2-Benzisothiazol-3(2H)-one (BIT) from Hand Surfaces Using an Isopropyl Alcohol/Water Wipe and Wash Procedure” (AEA08)

EPA conducted a science and ethics review of available information concerning the research

reported by the AEATF in “Determination of Removal Efficiency of 1,2-Benzisothiazol-3(2H)-one (BIT) from Hand Surfaces Using an Isopropyl Alcohol/Water Wipe and Wash Procedure,” also referred to as study AEA08. The HSRB reviewed the protocol for this study at the April 8-9, 2014 meeting. The study was conducted to measure the removal efficiency of the antimicrobial active ingredient BIT in latex paint and in isopropyl alcohol from human hands. The data from this study will be used to assess consumer and occupational exposure and risks from applying paint that contains antimicrobial pesticides. The charge questions and documents being transmitted to the HSRB for review are listed below.

The charge questions for the HSRB’s consideration are provided below:

Charge to the Board - Science:

- Did the research in study AEA08 generate scientifically reliable data, useful for establishing the efficiency of the hand wash procedure used to remove BIT-treated paint from the hands?

Charge to the Board - Ethics:

- Does the available information support a determination that the research was conducted in substantial compliance with the requirements of 40 CFR part 26, subpart Q?

Documents: EPA is providing for HSRB review the following documents:

- a) Science review of study AEA08
- b) Appendix A AEA08 Statistical Review
- c) Final AEA08 Data
- d) AEA08 Analysis – SAS Code
- e) Ethics review of study AEA08
- f) IRB Minutes & Roster
- g) AEATF Study Report – AEA08 Handwash Removal Efficiency

3) A completed study submitted by the AEATF: “A Study for Measurement of Potential Dermal and Inhalation Exposure During Application of a Latex Paint Containing an Antimicrobial Pesticide Product Using a Brush and Roller for Indoor Surface Painting” (AEA09)

EPA conducted a science and ethics review of available information concerning the research reported by the Antimicrobial Exposure Assessment Task Force II (AEATF II) in “A Study for Measurement of Potential Dermal and Inhalation Exposure During Application of a Latex Paint Containing an Antimicrobial Pesticide Product Using a Brush and Roller for Indoor Surface Painting,” also referred to as study AEA09. The HSRB reviewed the protocol for this study at the April 8-9, 2014 meeting. The study was conducted to determine the potential dermal and inhalation exposure to consumers associated with the applying latex paints containing antimicrobial pesticides using brushes and rollers. The data from this study will be used to assess consumer and occupational exposure and risks from applying paint that contains

antimicrobial pesticides. The charge questions and documents being transmitted to the HSRB for review are listed below.

The charge questions for the HSRB's consideration are provided below:

Charge to the Board - Science:

- Did the research in study AEA09 generate scientifically reliable data, useful for assessing the exposure of painters who apply paint containing antimicrobial pesticides using brushes and rollers?

Charge to the Board - Ethics:

- Does the available information support a determination that the research was conducted in substantial compliance with the requirements of 40 CFR part 26, subpart Q?

Documents: EPA is providing for HSRB review the following documents:

- a) Science review of study AEA09
 - b) Appendix A AEA09 Clothing PF Determination
 - c) Appendix B AEA09 Statistical Review
 - d) Final AEA09 Data
 - e) AEA09 Analysis – SAS Code
 - f) Ethics review of study AEA09
 - g) AEATF SOP Chapter 11
 - h) IRB Minutes & Roster
 - i) AEATF Study Report – AEA09 BIT Brush & Roller
- 4) **A published article titled: “Assessing key safety concerns of a *Wolbachia*-based strategy to control dengue transmission by *Aedes* mosquitoes”, authored by Jean Popovici, Luciano A Moriera, Anne Poinsignon, Inaki Iturbe-Ormaetxe, Darlene McNaughton, and Scott O’Neill**

EPA conducted a science and ethics review of the research presented in the article “Assessing key safety concerns of a *Wolbachia*-based strategy to control dengue transmission by *Aedes* mosquitoes,” as well as additional information available. This post-rule study enrolled human volunteers to provide blood meals to laboratory-reared mosquito colonies, some of which were infected with *Wolbachia* bacteria. Later, the research protocol was amended to evaluate whether mosquitoes transmit *Wolbachia* to humans through biting. EPA is considering citing this research as part of its human health risk assessment associated with registration of mosquitoes infected with *Wolbachia*. The HSRB is being asked to comment on this article.

The charge questions for the HSRB's consideration are provided below:

Charge to the Board - Science:

- Is the research described in the published article “Assessing key safety concerns of a *Wolbachia*-based strategy to control dengue transmission by *Aedes* mosquitoes” scientifically sound, providing reliable data for the purpose of contributing to a weight of evidence determination in EPA’s assessment of the risks to human health associated with releasing *Wolbachia*-infected mosquitoes?

Charge to the Board - Ethics:

- Does the available information support a determination that the research was conducted in substantial compliance with the requirements of 40 CFR part 26, subpart Q?

Documents: EPA is providing for HSRB review the following documents:

- a) Science review of article by Popovici et al.
- b) Ethics review of article by Popovici et al.
- c) IRB Package; O’Neill, S.L, I. Iturbe-Ormaetxe. 2011-2015. Institutional Approval Form for Experiments on Humans Including Behavioral Research. Rearing of Mosquitoes Using Blood from Human Volunteers 21/03/2011 – AMENDMENT. The University of Queensland.
- d) Emails between Michelle Arling (EPA Human Research Ethics Officer) and Scott O’Neill (corresponding author)
- e) National Statement on Ethical Conduct in Human Research (Australia)
- f) National Health and Medical Research Council Act 1992 (Australia)
- g) “Assessing key safety concerns of a *Wolbachia*-based strategy to control dengue transmission by *Aedes* mosquitoes”, authored by Jean Popovici, Luciano A Moriera, Anne Poinsignon, Inaki Iturbe-Ormaetxe, Darlene McNaughton, and Scott O’Neill