

October 10, 2018

EPA-HSRB-18-4

Dr. Jennifer Orme-Zavaleta  
Office of the Science Advisor  
1200 Pennsylvania Avenue, NW  
Washington, DC 20460

Subject: July 25, 2018 EPA Human Studies Review Board Meeting Report

Dear Dr. Orme-Zavaleta,

The United States Environmental Protection Agency requested that the Human Studies Review Board (HSRB) provide scientific and ethics reviews of one protocol in its July 2018 meeting. The protocol was entitled *Laboratory evaluation of mosquito bite protection from permethrin-treated clothing after 0, 50, 75, and 100 washings*. The Board's responses to the charge questions and detailed rationale and recommendations for this protocol are provided in the enclosed final meeting report.

Signed,

A handwritten signature in blue ink that reads "Edward E. Gbur, Jr.".

Edward E. Gbur, Jr., PhD  
Vice-Chair  
EPA Human Studies Review Board

## **INTRODUCTION**

On July 25, 2018, the United States Environmental Protection Agency's (EPA or Agency) Human Studies Review Board (HSRB or Board) met to address the scientific and ethical charge questions related to the following topic: A protocol entitled "Laboratory evaluation of mosquito bite protection from permethrin-treated clothing after 0, 50, 75, and 100 washings."

## **REVIEW PROCESS**

The Board conducted a public meeting on July 25, 2018. Advance notice of the meeting was published in the *Federal Register* as "Human Studies Review Board; Notification of a Public Meeting" (EPA, FRL-9980-61-ORD). This Final Report of the meeting describes the HSRB's discussion, recommendations, rationale and consensus in response to the charge questions on the ethical and scientific aspects of the above named protocol.

Agency staff presented their review of scientific and ethical aspects of the completed study, with each presentation followed by clarifying questions from the Board. The HSRB solicited public comments and then took up the charge questions under consideration. The Board discussed the science and ethics charge questions and developed a consensus response to each question in turn. For each of the charge questions, the Vice-Chair called for the Board to vote to confirm concurrence on a summary statement reflecting the Board's response.

For their evaluation and discussion, the Board considered presentations given by EPA staff at the meeting, oral comments from Agency staff and from the investigators during the meeting discussions, and a public comment, as well as the Agency's written reviews, which were provided to the Board prior to the meeting.

### **Science charge to the Board:**

Is the protocol entitled "Laboratory evaluation of mosquito bite protection from permethrin-treated clothing after 0, 50, 75, and 100 washings" likely to generate scientifically reliable data, useful for estimating the level of mosquito bite protection provided by the different textiles treated with permethrin?

### **Summary of the Board's questions for clarification:**

In response to Board members' questions for clarification on the method of loading permethrin onto a fabric and the actual amount loaded, EPA's understanding is that the variability in the amount of permethrin loaded onto the test fabrics would be controlled at 0.52% and the test fabrics would be a flame-resistant, Army combat uniform (FRACU) and an Army combat uniform (ACU) or similar fabrics, as well as some representative consumer fabrics. In addition, a Board member asked for clarification on whether or not there will be precisely 200 mosquitoes per test. EPA confirmed that to be the case.

### **Summary of the Board's science review:**

The Board's science reviewers did not have any serious concern about toxicology issues or the risk to subjects from chemical exposures. However, concern was again expressed about controlling the amount of permethrin loaded onto the fabric. A Pulcra representative responded that the permethrin would be

applied using a padding process and the loaded amount would be measured analytically. In addition, they indicated that they would also measure the residue at the end of the test. The reviewer recommended that more explicit details be included in the description of the protocol.

Since the test of the fabric washed 100 times would be conducted before those with fewer washings, the vice-chair questioned the need for the remaining washing level studies if the 100 wash level test maintained mosquito bite protection. A Board member indicated that he had previously recommended the test order be randomized. The Board consultant asked whether or not the Department of Defense was part of the approval process for the protocol. In addition, the consultant asked about the value of testing the mosquitoes for disease if they had been already certified as disease free. No statistical concerns were expressed by the statistics reviewer.

**Board recommendations:**

The Board made the following recommendations.

- More explicit details should be included in the protocol on how the amount of permethrin initially loaded onto the fabric will be determined and how the residue will be measured.
- Include justification in the protocol for starting with the 100 washing level test rather than randomizing the order of the washing level tests.
- Include justification in the protocol as to why starting with the 100 washing level test does not eliminate the need for testing at fewer washing levels.

**Public comment:**

A public comment was received from William Jordan who asked why it would be necessary to carry out tests with fewer than 100 washings if this would be the first test conducted. Assuming the loss of pesticide residue with each washing, a larger number of washings would appear to increase the subject's chance of being bitten by a mosquito.

**Board response to the science charge:**

The HSRB concluded that, subject to the modifications recommended by EPA and additional recommendations, changes and clarifications requested by the Board, the study is likely to generate scientifically reliable data, useful for estimating the level of mosquito bite protection provided by the different types of textiles treated with permethrin. The Board's questions for clarification and suggested changes were summarized above.

**Ethics charge to the Board:**

Is the protocol entitled "Laboratory evaluation of mosquito bite protection from permethrin-treated clothing after 0, 50, 75, and 100 washings" likely to meet the applicable requirements of 40CFR part 26, subparts K and L?

**Summary of the Board's questions for clarification:**

The Board ethics reviewer asked whether or not screening questions would be asked to ensure that nursing women would be excluded from participation. EPA responded that the issue would be addressed in a second conversation before the consent meeting. Nursing women would be excluded.

In response to the vice-chair's question about the need for an upper age limit of 55 years old for participation, EPA responded that they would have no objection to this age limit but would verify the rationale for including it in the protocol.

**Summary of the Board ethics review:**

The Board's ethics reviewer again questioned the need for the 55 year old age limit for study participants. The reviewer also recommended that it be made clear to participants during the selection process that the mosquitoes to be used in the studies will be certified as disease free.

In response to the reviewer's concern about reuse of mosquitoes from the subject's preliminary attractiveness phase for inclusion in the test. EPA indicated that the subject's arm would have a physical barrier between it and the mosquitoes during that phase. However, when i2L was asked about this issue, they indicated that the subject's arm would be in the cage with mosquitoes during the attractiveness phase but that if a mosquito did land on the fabric during the attractiveness phase the technician monitoring the test would prevent it from probing or biting.

In the discussion that Pulcra's payment of medical expenses resulting from injury to a participant would be paid if the subject's regular health insurer did not cover the expenses, the reviewer questioned the reason that the subject's regular insurer should pay the claim. EPA indicated the point was valid but felt that injuries to a participant were uncommon.

**Board recommendations:**

The Board made the following recommendations

- All edits outlined in the EPA's science and ethics review of the protocol should be incorporated.
- The age limit for participation should be justified or removed from the protocol.
- Clarification and additional information on the attractiveness phase should be provided in the protocol regarding whether a subject's arm will be exposed to mosquitos or whether there will be a physical barrier between the mosquitos and the subject's arm.
- The protocol should make it clear during the participant screenings that the mosquitoes used in the tests have been certified as disease free.
- A rationale for the participant's health insurance to be the primary provider of coverage should an injury occur during the test should be included in the protocol.

**Board response to the ethics charge:** The HSRB concluded that, subject to the modifications recommended by EPA and additional changes and clarifications made by the Board, the study is likely to meet the applicable requirements of 40CFR part 26, subparts K and L. The Board's suggested changes and recommendations for clarifications are described above.

**Voting and adjournment:**

The Board formally voted unanimously to accept their science and ethics responses as stated above, subject to the clarifications and justifications described in the discussion summaries. The meeting was then adjourned.