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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

March 20, 2014

MEMORANDUM

SUBJECT: Materials for Review by the Human Studies Review Board for its April 8-9, 2014 Meeting

TO: Jim Downing
Designated Federal Official
Human Studies Review Board
Office of Science Advisor (8105R)

FROM: William L. Jordan
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This memorandum describes 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 meeting scheduled for April 8-9, 2014. At this meeting, EPA will ask the Board to address scientific and ethical issues surrounding these four topics, each of which is discussed further below:

1. A new scenario design and associated protocol from the Antimicrobial Exposure Assessment Task Force II (AEATF-II) describing proposed research to monitor dermal and inhalation exposure during manual pouring of solid formulation antimicrobial products.[1]

2. A new scenario design and associated protocol from the AEATF-II describing proposed research to monitor dermal and inhalation exposure during application of latex paint containing an antimicrobial pesticide product using brush and roller equipment.

3. A new protocol from the AEATF-II describing proposed research to measure the removal efficiency of 1,2-Benzisothiazol-3(2H)-one (known as BIT) from hand surfaces using an isopropyl alcohol/water wipe and wash procedure.

[1] This topic was originally scheduled for review by the HSRB on October 1, 2013, but that meeting was cancelled as a result of the federal government shutdown that occurred from October 1-16, 2013.

4. A new protocol from the U.S. Department of Agriculture describing proposed research to determine the bite protection level of repellent-treated clothing for the United States Military

In addition to presenting its reviews of the four topics listed above, the EPA will also present background information about EPA's Repellency Awareness Program and discuss potential implications for the HSRB. No background documents are being provided on this topic, and there are no charge questions for consideration by the Board. The Agency expects to provide its presentation to the Board members in advance of the meeting.

1. AEATF II Protocol – Manual Pouring of Solid Formulation:

First, the Board will consider a new scenario design and associated protocol from the Antimicrobial Exposure Assessment Task Force II (AEATF-II) describing proposed research to monitor dermal and inhalation exposure during manual pouring of solid formulation antimicrobial products. Because the proposed research involves scripted exposure, it meets the regulatory definition of "research involving intentional exposure of a human subject" and thus is covered by subparts K and L of EPA's amended rule for the protection of human subjects of research. The rule at 40 CFR §26.1125 requires a sponsor or investigator to submit to EPA, before conducting a study involving intentional exposure of human subjects, the protocol and related materials describing the proposed human research. In addition, EPA's regulation at 40 CFR §26.1601 requires EPA to perform science and ethics reviews of the submitted proposal and to seek HSRB review of the proposed research. EPA has reviewed the scenario design and protocol, and has concluded that the research, with minor revisions, is likely to generate scientifically sound, useful information and to meet the applicable provisions of the EPA regulations in 40 CFR part 26, subparts K and L. The charge questions and documents being transmitted to the HSRB for review are listed below.

Charge Questions for AEATF-II Protocol:

If the AEATF-II study proposal AEA07 is revised as suggested in EPA's review and if the research is performed as described:

1. Is this research is likely to generate scientifically reliable data, useful for assessing the exposure of those who pour solid formulation antimicrobial pesticide products

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

Documents for AEATF-II Solid Pour Protocol Review:

EPA is providing for HSRB review the following 9 files concerning the AEATF-II protocol AEA07. These files were released in September 2013, in preparation for the HSRB meeting on October 1, 2013. The files are being re-released at this time, for the convenience of the HSRB members.

a. EPA Science and Ethics Review of AEATF-II Solid Pour Scenario Design and Protocol for Exposure Monitoring (dated September 10, 2013)

b. Volume 1: AEATF-II Pour Solid Protocol Submission
- AEATF-II's Transmittal Letter
- 40 CFR 26.1125 Checklist
- Pour Solid Study Design Document

c. Volume 2: AEATF-II Pour Solid Protocol Submission
- Study Protocol Dated 4/26/13, Approved 4/29/13
- Approved Occupational Monitoring Informed Consent Form Dated 4/29/13
- Approved Residential Monitoring Informed Consent Form Dated 4/29/13
- Approved Spanish Translation of Informed Consent Forms dated 4/29/13
- Approved Recruitment Materials Dated 5/1/13
- Approved Spanish Translation of Recruitment Materials Dated 5/1/13
- Schulman Associates IRB (SAIRB) Approval Letter and Supporting Documents

d. Volume 3: AEATF-II Pour Solid Protocol Submission
- Records of SAIRB Review of Study AEA07 and Correspondence
- SAIRB Meeting Minutes

e. Volume 4: AEATF-II Pour Solid Protocol Submission
- CVs and Ethics Training Records
- AEATF II Standard Operating Procedures (SOPs) Referenced in AEA07 Protocol

f. AEATF II Supplemental Submission of Toxicity Study Summaries for Cyanuric Acid (CYA)

g. Schulman Associates IRB Standard Operating Procedures (dated December 2012)

h. Schulman Associates IRB Board Members for 2013

i. Charge Questions

2. <u>AEATF II Protocol – Brush and Roller Painting:</u>

Second, the Board will consider a new scenario design and associated protocol from the AEATF-II describing proposed research to monitor dermal and inhalation exposure to individuals who apply latex paint containing antimicrobial pesticide products with brush and roller equipment. Because the proposed research involves scripted exposure, it meets the regulatory definition of "research involving intentional exposure of a human subject" and thus is covered by subparts K and L of EPA's amended rule for the protection of human subjects of research. The rule at 40 CFR §26.1125 requires a sponsor or investigator to submit to EPA, before conducting a study involving intentional exposure of human subjects, the protocol and related materials describing the proposed human research. In addition, EPA's regulation at 40 CFR §26.1601 requires EPA to perform science and ethics reviews of the submitted proposal and

to seek HSRB review of the proposed research. EPA has reviewed the scenario design and protocol, and has concluded that the research, with minor revisions, is likely to generate scientifically sound, useful information and to meet the applicable provisions of the EPA regulations in 40 CFR part 26, subparts K and L. The charge questions and documents being transmitted to the HSRB for review are listed below.

Charge Questions:

If the AEATF-II study proposal AEA09 is revised as suggested in EPA's review and if the research is performed as described:

1. Is this research is likely to generate scientifically reliable data, useful for assessing the exposure of those who apply latex paint containing an antimicrobial pesticide using a brush or roller?

2. 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 11 documents:

a. EPA Science and Ethics Review of AEATF-II Brush and Roller Painting Scenario Design and Protocol for Exposure Monitoring (dated March 14, 2014)

b. Volume 1: AEATF-II Brush and Roller Protocol Submission
- AEATF-II's Transmittal Letter
- 40 CFR 26.1125 Checklist
- Study Design Document

c. Volume 2: AEATF-II Brush and Roller Protocol Submission
- Draft study protocol dated 1/22/14
- Draft informed consent form dated 1/22/14
- Draft recruitment materials dated 1/22/14
- Schulman Associates IRB (SAIRB) Conditional Approval Letter
- California Department of Pesticide Regulation (CDPR) review and response documentation

d. Volume 3: AEATF-II Brush and Roller Protocol Submission
- Records of SAIRB Review of Study AEA09 and Correspondence
- CDPR Communications

e. Volume 4: AEATF-II Brush and Roller Protocol Submission
- AEATF-II SOPs Referenced in AEA09 Protocol

f. Statistics file: Fold accuracy (LST file)

g. Statistics file: Fold accuracy (SAS file)

h. Statistics file: Power (LST file)

i. Statistics file: Power accuracy (SAS file)

j. Schulman Associates IRB Standard Operating Procedures (dated December 2012)

k. Charge Questions

3. AEATF II Protocol – Removal Efficiency Study Protocol:

Third, the Board will consider a new protocol from the AEATF-II describing proposed research to measure the removal efficiency of the antimicrobial active ingredient 1,2-Benzisothiazol-3(2H)-one (BIT) in latex paint and in isopropyl alcohol from human hands. Because the proposed research involves scripted exposure, it meets the regulatory definition of "research involving intentional exposure of a human subject" and thus is covered by subparts K and L of EPA's amended rule for the protection of human subjects of research. The rule at 40 CFR §26.1125 requires a sponsor or investigator to submit to EPA, before conducting a study involving intentional exposure of human subjects, the protocol and related materials describing the proposed human research. In addition, EPA's regulation at 40 CFR §26.1601 requires EPA to perform science and ethics reviews of the submitted proposal and to seek HSRB review of the proposed research. EPA has reviewed the scenario design and protocol, and has concluded that the research, with minor revisions, is likely to generate scientifically sound, useful information and to meet the applicable provisions of the EPA regulations in 40 CFR part 26, subparts K and L. The charge questions and documents being transmitted to the HSRB for review are listed below.

Charge Questions:

If the AEATF-II study proposal AEA08 is revised as suggested in EPA's review and if the research is performed as described:

1. Is this research likely to generate scientifically reliable data, useful for determining the removal efficiency of BIT from the hands due to dermal exposure associated with the use of latex paint and non-paint liquid solutions containing containing BIT?

2. 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 7 documents:

a. EPA Science and Ethics Review of AEATF-II Removal Efficiency Study Protocol (dated March 18, 2014)

b. Volume 1: AEATF-II Removal Efficiency Study Protocol Submission
- AEATF-II's Transmittal Letter
- 40 CFR 26.1125 Checklist

c. Volume 2: AEATF-II Removal Efficiency Study Protocol Submission

- Draft study protocol dated 1/23/14
- Draft informed consent form dated 1/23/14
- Draft recruitment materials dated 1/23/14
- Schulman Associates IRB (SAIRB) Conditional Approval Letter
- California Department of Pesticide Regulation (CDPR) review and response documentation

d. Volume 3: AEATF-II Removal Efficiency Study Protocol Submission

- Records of SAIRB Review of Study AEA08 and Correspondence
- CDPR Communications

e. Volume 4: AEATF-II Removal Efficiency Study Protocol Submission

- AEATF-II SOPs Referenced in AEA08 Protocol

f. Schulman Associates IRB Standard Operating Procedures (dated December 2012)

g. Charge Questions

4. USDA Protocol – Evaluation of Bite Protection from Repellent-Treated Clothing for the United States Military:

Fourth, the Board will consider a new protocol from the U.S. Department of Agriculture describing proposed research to determine the bite protection level provided by etofenprox-treated U.S. Military Fire Resistant Army Combat Uniforms (FRACUs). Because the proposed research involves scripted exposure, it meets the regulatory definition of "research involving intentional exposure of a human subject" and thus is covered by subparts K and L of EPA's amended rule for the protection of human subjects of research. The rule at 40 CFR §26.1125 requires a sponsor or investigator to submit to EPA, before conducting a study involving intentional exposure of human subjects, the protocol and related materials describing the proposed human research. In addition, EPA's regulation at 40 CFR §26.1601 requires EPA to perform science and ethics reviews of the submitted proposal and to seek HSRB review of the proposed research. EPA has reviewed the scenario design and protocol, and has concluded that the research, with minor revisions, is likely to generate scientifically sound, useful information and to meet the applicable provisions of the EPA regulations in 40 CFR part 26, subparts K and L. The charge questions and documents being transmitted to the HSRB for review are listed below.

Charge Questions:

If the USDA study proposal is revised as suggested in EPA's review and if the research is performed as described:

1. Is the protocol "Laboratory Evaluation of Bite Protection From Repellent Impregnated Clothing for the United States Military" likely to generate scientifically reliable data, useful

for estimating the level of mosquito bite protection provided by two different textiles treated with etofenprox?

2. 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 7 documents:

a. EPA Science and Ethics Review of USDA Protocol to Evaluate Bite Protection from Repellent-treated clothing for the United States Miliary (dated March 19, 2014)

b. Volume 1: USDA Protocol Submission
- Protocol dated 2/28/14 (approved by Western Institutional Review Board (WIRB) on 3/4/14)
- WIRB-approved informed consent form
- WIRB-approved recruitment materials
- WIRB Approval Letter

c. Volume 2: USDA Protocol Submission
- Records of WIRB Review

d. Volume 3: USDA Protocol Submission
- Statistical Methods: Supplemental Information

e. WIRB SOPs and Policies

f. WIRB Meeting Minutes

g. Charge Questions