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

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

October 3, 2011

MEMORANDUM

SUBJECT: Materials for Review by the Human Studies Review Board for its October 19-20, 2011 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 October 19-20, 2011. 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) describing proposed research to determine potential dermal and inhalation exposures associated with the manual pouring of liquid antimicrobial products.

2. A new scenario design and associated protocol from the Agricultural Handler Exposure Task Force (AHETF) describing proposed research to monitor exposure of workers who perform closed system loading of liquids in non-returnable and returnable containers.

3. A completed Carroll-Loye Biological Research, Inc., field efficacy study of a PMD- and lemongrass oil-based repellent 'No Mas' against mosquitoes.

4. A published report (Moiemen et al. 2011) of an intentional exposure human study measuring dermal absorption of silver from nanosilver.

1. Proposed AEATF research on exposure associated with the manual pouring of liquid antimicrobial products (AEA05).

In several previous meetings, the HSRB has considered the design and conduct of research to measure the levels of exposure received by professionals who mix, load, or apply pesticides using various types of equipment. Both agricultural and antimicrobial pesticide handler scenarios have been considered. At this meeting, the Board will consider a proposal for research monitoring exposure of workers who perform manual open pouring of liquid 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 for AEA05, 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.

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

a. EPA Science and Ethics Review
b. Submission Documents
    1. Volume 1: Transmittal Letter, Checklist, Study Design Document
    2. Volume 2: Protocol, IRB Approval Letter, Supporting Documents
    3. Volume 3: IRB Review Records
    4. Volume 4: CVs and Ethics Training Records, SOPs
c. Reference Files
    1. AEATF Governing Document, Version 3 (dated 7-08-11)
    2. IIRB, Inc. Human Research Protection Plan (dated 11-3-10)
    3. IIRB, Inc. Current Membership Roster (dated 9-12-11)

Charge Questions:

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

1. Is the research likely to generate scientifically reliable data, useful for assessing the exposure of individuals who manually pour liquid antimicrobial products?

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

2. Proposed AHETF research on Exposure Monitoring of Workers During Closed System Loading of Returnable and Non-Returnable Containers.

At this meeting, the Board will also consider a proposal for research monitoring the potential exposure of workers using closed systems to load liquid pesticide products from returnable or nonreturnable containers into mix or spray tanks. 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.

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

a. EPA Science and Ethics Review
b. Submission Document
    1. Monitoring Unit Selection and Construction Plan, SOPs, IRB Review Records
c. Reference Files
    1. AHETF Governing Document Version 2 - August 2010
    2. IIRB, Inc. Human Research Protection Plan 11-3-10
    3. IIRB, Inc. Current Membership Roster 9-12-11

Charge Questions:

1. Is the research likely to generate scientifically reliable data, useful for assessing the exposure of workers using closed systems to load liquid pesticide products from returnable or nonreturnable containers?

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

3. Report of Completed Carroll-Loye Biological Research, Inc. Study No Mas-003: Field Efficacy Test of a PMD and Lemongrass Oil-Based Repellent 'No Mas' Against Mosquitoes

The Board will also be reviewing the unpublished report of a completed Carroll-Loye Biological Research, Inc. study No Mas 003: Field Efficacy Test of a PMD and Lemongrass Oil-Based Repellent 'No Mas' Against Mosquitoes. The protocol for this study was reviewed favorably by the HSRB at their meeting in October 2010. EPA seeks the advice of the HSRB on the scientific soundness of this completed study for use to estimate the duration of complete protection against mosquitoes provided by the tested repellent, and on whether available information supports a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR Part 26.

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

1. EPA Reviews
    i. EPA Science Review – No Mas Completed Study
    ii. EPA Ethics Review – No Mas Completed Study
2. Background Documents
    i. No Mas 003 Final Report (8-14-11)
    ii. Explanation re Statistical Programs Used (from Scott Carroll)
    iii. Data – No Mas 003 CPT for survival (file in Excel)
3. Reference Files
    i. CLBR Protocol Submission - No Mas 003 (7-15-10)
    ii. EPA Science and Ethics Review of No Mas PROTOCOL (10-1-10)
    iii. IIRB, Inc. Human Research Protection Plan 11-3-10
    iv. IIRB, Inc. Current Membership Roster 9-12-11

Charge Questions:

1. Is the CLBR completed study No Mas 003 sufficiently sound, from a scientific perspective, to be used to estimate the duration of complete protection against mosquitoes provided by the tested repellent?

2. Does available information support a determination that the studies were conducted in substantial compliance with 40 CFR Part 26, subparts K and L?

4. A published report (*Moiemen* et al. 2011) of an intentional exposure human study measuring dermal absorption of silver from nanosilver.

In April 2011, the HSRB reviewed a published report (*Gulson* et al. 2010) of an intentional exposure human study measuring dermal absorption of zinc oxides contained in sunscreens. At the upcoming meeting in October 2011, the HSRB will be reviewing another published report that also provides information that is potentially relevant to assessing the impacts of nanomaterials on human health and the environment. The study, *Moiemen* et al 2011, examines dermal absorption of silver in burn patients treated with wound dressings containing nanosilver. EPA is interested in the *Moiemen* study because it could potentially be used to support dermal exposure assessments for pesticide formulations that contain nanosilver.

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

a. EPA Reviews
    1. EPA Science Review of Moiemen 2011 MRID 48607501
    2. EPA Ethics Review of Moiemen 2011 MRID 48607501
b. Background Document
    1. Moiemen et al. 2011 (MRID 48607501)
c. Reference Files: Ethics Approval Records
    1. Volume 1: Smith & Nephew Response to Questions from US EPA (9/19/11)
    2. Volume 2: Ethics Application #1 to Sandwell and West Birmingham Local Research Ethics Committee (11/22/05)

3. Volume 3: Response to Ethics Application #1 (not approved) (1/17/06)
4. Volume 4: Ethics Application #2 to Sandwell and West Birmingham Local Research Ethics Committee (1/27/06)
5. Volume 5: Response to Ethics Application #2 (revisions requested) (3/10/06)
6. Volume 6: Response back to Sandwell and West Birmingham Local Research Ethics Committee (revisions/additional information) (3/14/06)
7. Volume 7: Approval of Ethics Application #2 (approval of research) (4/05/06)
8. Volume 8: Protocol Amendments 2, 3 (10/25/06)
9. Volume 9: Protocol Amendment 4 (3/06/07)

Charge Questions:

1. Is the Moiemen et al. (2011) study scientifically sound, providing reliable data?

2. If so, can the Moiemen et al. (2011) study be used to support the Agency's conclusion that the dermal absorption factor for silver from nanosilver on human skin is less than 0.1%?

3. Is there adequate information to support a determination that the study was conducted in substantial compliance procedures at least as protective as those at subparts A-L of 40 CFR Part 26?