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WASHINGTON D.C., 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

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MEMORANDUM

SUBJECT: Materials for review by the Human Studies Review Board for its October 2010 Meeting

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

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This memorandum describes the materials OPP is providing for review by the Human Studies Review Board (HSRB or Board) at the meeting scheduled for October 27-28, 2010. At this meeting EPA will ask the Board to address scientific and ethical issues surrounding these topics, each of which is discussed further below:

1. A proposal for new research to be conducted by Carroll-Loye Biological Research to evaluate in the field the repellent efficacy to mosquitoes of an unregistered product "No Mas" containing 16% Para-menthane-3,8-diol (PMD) and 2% Lemongrass oil.
2. A new scenario design and associated protocol from the Agricultural Handler Exposure Task Force (AHETF), describing proposed research to monitor at 7 sites the exposure of experienced workers who apply herbicides for vegetation control in utility rights-of-way using backpack or hand-gun sprayers.
3. A report from the Antimicrobials Exposure Assessment Task Force II (AEATF-II) of completed research monitoring the exposure of janitorial workers cleaning floors with an antimicrobial pesticide applied with a bucket and mop.

4. An amended scenario design and associated protocol from the Agricultural Handler Exposure Task Force (AHETF), describing proposed research to monitor at 5 sites the exposure of experienced workers who mix and load pesticides formulated in water-soluble packaging.

1. Proposed CLBR Mosquito Repellent Study No Mas-003 with formulation containing PMD and Lemongrass Oil.

In earlier meetings the HSRB has reviewed proposals from Carroll-Loye Biological Research (CLBR) for several field studies of mosquito repellency of various formulations. This new proposal, No Mas-003, is for a field study of the repellency to mosquitoes of a new repellent product containing 16% Para-menthane-3,8-diol (PMD) and 2% Lemongrass oil. Apart from the new test material, the proposal is generally similar to previous Carroll-Loye field studies reviewed by the Board.

EPA's regulation at 40 CFR §26.1125 requires a sponsor or investigator to submit to EPA, before conducting a study involving intentional exposure of human subjects, a protocol and supporting 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 submitted proposals, and to seek HSRB review of the proposed research. Because the proposed research involves exposure of subjects that would not occur but for their participation in the research, it meets the regulatory definition of "research involving intentional exposure of a human subject," and thus these provisions of regulation apply to it.

EPA has reviewed both the scientific and ethical aspects of Carroll-Loye protocol No Mas-003, and has concluded that, with minor revisions, it 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.

1. EPA is providing for HSRB Review the following materials on the proposed Carroll-Loye mosquito repellent efficacy study No Mas-003:
 - a. CLBR Protocol No Mas-003 (7/15/10)
 - b. EPA Science and Ethics Review of No Mas-003 (10/1/10)

Charge Questions:

If the proposed field repellency study protocol No Mas-003 is revised as suggested in EPA's review and if the research is performed as described:

- a. Is the research likely to generate scientifically reliable data, useful for assessing the efficacy of the tested material in repelling mosquitoes?
- b. Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

2. Proposed AHETF research on exposure of workers applying pesticides for vegetation control in rights of way using backpack or hand gun sprayers.

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 two companion proposed handler exposure scenarios involving workers who apply herbicides for vegetation control in utility rights of way. This proposal is generally similar to others the Board has seen before from the Agricultural Handler Exposure Task Force (AHETF), but differs in some important ways.

This new proposal describes two similar but distinct scenarios, both involving application of herbicides in rights of way. One scenario involves application using a backpack sprayer; the other involves application using a handgun sprayer. Each scenario calls for collection of samples from three workers at each of seven sites, for a total of 21 Monitoring Units (MUs) for each scenario, and 42 MUs in all.

When the scenario is complete, the resulting data will be posted to the Agricultural Handler Exposure Database (AHED[®]). EPA intends to use these data generically to estimate daily dermal and inhalation exposures of pesticide handlers who apply pesticides in these use scenarios. Data from this research addressing exposure from spraying only can be combined with data from an appropriate mixing/loading scenario to estimate exposures of pesticide handlers who both mix/load and apply.

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 AHETF Rights of Way Application scenario definitions and the associated protocol AHE400, and has concluded that they are likely to generate scientifically sound, useful information and, with minor revisions, to meet the applicable provisions of the EPA regulations in 40 CFR part 26, subparts K and L.

2. EPA is providing for HSRB review the following materials concerning the AHETF proposal for monitoring applicators using backpack or handgun sprayers to apply herbicides in utility rights of way:
 - a. Final Submission for Review of AHE400 (6-18-10)
 - b. Supplement 1: SOPs cited in AHE400

- c. Supplement 2: Providing Individual Exposure Information to Subjects
- d. Supplement 3: Explanation of AHETF Spanish translation project
- e. EPA Science & Ethics Review AHE400 ROW Final (9-30-10)

Charge Questions:

If the proposed AHETF Right-of-Way application scenario and field study proposal AHE400 is revised as suggested in EPA's review and if the research is performed as described:

- a. Is the research likely to generate scientifically reliable data, useful for assessing the exposure of workers who apply pesticides in utility rights of way using backpack or handgun sprayers?
- b. Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?

3. Completed AEATF II research on exposure of workers applying antimicrobial pesticides to floors using mop and bucket.

In its meeting in April 2008 the HSRB reviewed favorably a proposal from the Antimicrobial Exposure Assessment Task Force II (AEATF II) for research to measure the levels of dermal and inhalation exposure received by professional janitorial workers who clean floors with an antimicrobial pesticide product using a mop and bucket. After revisions to address EPA, HSRB, and California DPR comments, this research was conducted in the summer of 2009 and reported and submitted to EPA in the summer of 2010.

At this meeting the Board will review the reports of this completed work, the first scenario to be completed by the AEATF II.

If the data for the Mop Scenario are accepted by EPA, the resulting data will be posted to the Biocide Handlers Exposure Database (BHED[®]). EPA intends to use these data generically to estimate daily dermal and inhalation exposures of those who clean floors with antimicrobial pesticides using a mop and pail. Data from this scenario addressing exposures from mopping and dumping the spent mop solution can be combined with data from an appropriate mixing/loading scenario to estimate exposures of workers who both mix/load and apply.

Because this research involved scripted exposure, it meets the regulatory definition of "research involving intentional exposure of a human subject" and thus was covered by subparts K and L of EPA's amended rule for the protection of human subjects of research. The rule at 40 CFR §26.1303 requires the submitter of reports of completed human research to document its ethical conduct. The rule at 40 CFR §26.1602(a) requires EPA to "review the material submitted under §26.1303 and other available, relevant information, and [to] document its conclusions

regarding the scientific and ethical conduct of the research.” The rule at 40 CFR §26.1602(b) further requires EPA to submit the data and EPA’s review to the HSRB if it decides to rely on the data.

EPA has reviewed the AEATF II Mop Scenario report and supplements and has concluded that it provides scientifically sound, useful information, and was conducted in substantial compliance with 40 CFR part 26, subparts A through L.

- 3. EPA is providing for HSRB review the following materials concerning the completed AEATF II study of the exposure of workers who use antimicrobial pesticides to clean floors using a mop and pail.

- a. MRID 48210201 Mop Study Final Report (7-28-10)

Note that Appendices Q and R, pp. 583-2116, are superseded by pp. 163-1146 in Supplement 1

- b. MRID 48231201 Supplement 1 to Mop Study Final Report

Includes protocol with tracked changes, more detailed chronology, and more complete, indexed versions of Appendices Q and R.

- c. MRID 48231901 Supplement 2 to Mop Study Final Report

Explains rationale for leaving ME stratum definitions unchanged in spite of HSRB comments

- d. EPA Ethics Review of AEATF Mop Study (10-4-10)

- e. EPA Science Review of AEATF Mop Study (10-4-10)

Statistics Supplement to EPA Science Review:

- a. J. Cohen Statistical Analysis (9-28-10)
- b. AEATF Mop Stats SAS File
- c. Mopsummary092810 – input to SAS code
- d. Mop.summary.results.092810
- e. Instructions for Replicating Statistical Analysis

Additional reference files:

- f. EPA Science & Ethics Review of Mop Study Proposal (3-10-08)

- g. HSRB Comments on Mop Study Proposal (6-25-08)

- h. IIRB, Inc., Roster and Procedures

i. AEATF II SOPs

Charge Questions:

- a. Was the research reported in the Antimicrobial Exposure Assessment Task Force II (AEATF–II) completed study report AEA03 and associated supplemental reports faithful to the design and objectives of the protocol and governing documents of AEATF-II?
- b. Has the Agency adequately characterized, from a scientific perspective, the limitations on these data that should be considered when using the data in estimating exposure of those who apply antimicrobial floor-cleaning products with mop and bucket?
- c. Does available information support a determination that the study was conducted in substantial compliance with subparts K and L of 40 CFR Part 26?

4. Revised proposal for AHETF research on exposure of workers mixing/loading pesticides in water-soluble packaging.

The Agricultural Handler Exposure Task Force (AHETF) has submitted a revised proposal for research on dermal and inhalation exposures of workers who mix and load pesticides formulated in water-soluble packaging. The original design and protocol for this scenario were reviewed favorably by the HSRB in June 2009. The AHETF has since revised them to use different surrogate chemicals. Those changes forced other revisions in turn; taken together, the proposed changes are significant enough to warrant a new review of the revised proposal by the HSRB.

- 4. EPA is providing for HSRB review the following materials concerning the revised AHETF proposal for monitoring workers who mix and load pesticides in water-soluble packaging:
 - a. AHE120 Mix-Load WSP Revised Scenario (8-19-10)
 - b. Supplement 1: SOPs cited in AHE120
 - c. Supplement 2: Providing Individual Exposure Information to Subjects
 - d. Supplement 3: Explanation of AHETF Spanish translation project
 - e. EPA Science & Ethics Review of Rvsd AHE120 M-L WSP (10-1-10)

Additional reference Files:

- f. EPA Science & Ethics Rvw of Original AHE120 Proposal (4-8-09)
- g. HSRB Comments on Original AHE120 Proposal (10-26-09)

Charge Questions:

If the revised AHETF scenario and field study proposal AHE120 is revised as suggested in EPA's review and if the research is performed as described:

- a. Is the research likely to generate scientifically reliable data, useful for assessing the exposure of handlers who mix and load pesticides in water-soluble packaging?
- b. Is the research likely to meet the applicable requirements of 40 CFR part 26, subparts K and L?