

US EPA ARCHIVE DOCUMENT

June 6, 2006

**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
HUMAN STUDIES REVIEW BOARD (HSRB)**

**June 27 – 30, 2006
PUBLIC MEETING**

**U.S. Environmental Protection Agency
One Potomac Yard (South Building)
2777 South Crystal Drive
Arlington, VA 22202
703-305-7090**

**HSRB WEB SITE <http://www.epa.gov/osa/hsrb/>
Docket Telephone: (202) 566-1752
Docket Number: EPA-HQ-ORD-2006-0384**

CHARGE TO THE BOARD

Part I: Chloropicrin

Chloropicrin is a non-selective soil fumigant whose primary toxic effect is sensory irritation in which stimulated free nerve endings mediate sensations and clinical signs in the nose, eyes, throat, and upper respiratory tract. Chloropicrin is a unique soil fumigant in that it is also used as an indicator chemical or warning agent (2% or less by weight in formulations). The Agency is developing an assessment to estimate inhalation risk to bystanders and workers from acute exposures to chloropicrin.

1. Scientific considerations:

The Agency's "Weight of Evidence" (WOE) document and Data Evaluation Records (DER) for chloropicrin describe the study design of the acute inhalation, human toxicity study. The Agency has concluded that the human toxicity study is appropriate for developing a point of departure for extrapolation of inhalation risk to bystanders and workers exposed to chloropicrin.

Please comment on whether the study is sufficiently sound, from a scientific perspective, to be used to estimate a safe level of inhalation exposure to chloropicrin.

2. Ethical considerations:

The Agency requests that the Board provide comment on the following:

- a. Is there clear and convincing evidence that the conduct of the Cain study was fundamentally unethical?
- b. Is there clear and convincing evidence that the conduct of the study was significantly deficient relative to the ethical standards prevailing at the time the research was conducted?

Part II: Research on the Efficacy of Insect Repellents

1. Insect Repellent Product Performance Testing Guideline

The U.S. EPA Office of Pesticide Programs requests that the HSRB review and comment on the draft “Product Performance of Skin-Applied Repellents of Insects and Other Arthropods” Testing Guideline in order to determine what changes, if any, are necessary for the guideline to be made consistent with the requirements for protection of human research subjects set forth in 40 CFR part 26. Below is a list of questions that focus on these topics.

- a. What actions should an investigator routinely take to minimize the risks to human subjects exposed during laboratory and field research on the efficacy of repellents?
- b. What types of toxicity data should be routinely generated before an investigator conducts repellent efficacy testing on human subjects with a new product?
- c. In private and university research laboratories, investigators themselves have sometimes served as research subjects when assessing chemicals for insect repellent activity. What scientific and ethical issues would such a practice raise? Under what conditions, if any, would such a practice be acceptable?
- d. Please comment on the scientific and ethical issues arising from the use of (or decision not to use) negative controls groups in repellent efficacy studies, in both laboratory and field studies.
- e. Please comment on the scientific and ethical issues raised by the design of studies to collect data sufficient to support assessment of repellent efficacy using the two different efficacy metrics: time to first confirmed bite (TFCB), and time providing x% protection of treated subjects from bites relative to untreated controls (RP).
- f. Please comment on appropriate approaches for estimating the minimum number of subjects needed to evaluate the level of efficacy of a repellent in laboratory and field studies.

g. Please comment on whether or not investigators should have an ethical obligation to provide subjects of repellent efficacy research with insurance to cover possible future medical costs or other losses that result from injury or illness experienced by the subjects as a consequence of their participation in the research.

h. Please comment on any special considerations that should be addressed in the informed consent materials provided people who are candidates to become subjects in insect repellent efficacy research.

i. Does the HSRB recommend that the draft guideline be revised? If so, please explain what aspects or sections might improve with revision.

2. *Study EMD-003 from Carroll-Loye Biological Research*

a. Does the proposed research described in [name / designation of the protocol] appear likely to generate scientifically reliable data, [useful for assessing the efficacy of the repellent] / [useful (together with other data) assessing the potential levels of pesticide exposure received by people when mixing, loading or applying a pesticides]?

b. Does the proposed research described in Study EMD-003 from Carroll-Loye Biological Research appear to comport with the applicable requirements of 40 CFR part 26, subparts K and L?

3. *Study EMD-004 from Carroll-Loye Biological Research*

a. Does the proposed research described in Study EMD-004 from Carroll-Loye Biological Research appear likely to generate scientifically reliable data, useful for assessing the efficacy of a test substance for repellent ticks?

b. Does the proposed research described in Study EMD-004 from Carroll-Loye Biological Research appear to comport with the applicable requirements of 40 CFR part 26, subparts K and L?

Part III: Research on Agricultural Handlers' Exposure to Pesticides

The Agricultural Handlers Exposure Task Force (AHETF) has submitted protocols for five pesticide exposure studies that are part of a larger research program the AHETF is conducting. The premise of the AHETF research program is that data can be used generically by various stakeholders (e.g., applicants, registrants, EPA, and others) for calculating exposures for the occupational handlers of pesticides. The scope of the AHETF research program is very broad in that it intends to address exposures related to many job functions in agriculture and also to assess generally the impacts of various parameters on exposure (e.g., How do changes in the pounds of pesticide handled or acres treated affect exposure levels?). The protocols submitted for HSRB review describe studies to measure exposures for five specific scenarios (i.e., closed or open system mixing/loading, airblast applications to trellis and orchard crops, or pilot exposures from fixed wing agricultural aircraft).

The Agency believes these studies improve EPA's ability to assess the risks of using pesticides because the data will reflect current agricultural practices, equipment and techniques and will allow for more refined exposure estimates. Further, the monitoring techniques to be used for these studies also have been standardized for use across the AHETF research program.. These more refined and reliable data will allow the Agency to estimate better how worker exposure levels are affected by changes in various factors such as the amount of active ingredient handled, type of application equipment used, application rate used, volumes handled, and personal protective equipment used.

It should be noted, however, that the use of the data generated in this study by the U.S. EPA and other stakeholders will depend upon the nature of the results. For example, the adequacy of the field or laboratory quality control data may dictate that correction factors are applied to adjust monitored exposure levels to account for losses from field samplers or low performing analytical methods.

1. AHETF Closed System Mixing/ Loading of Liquids Protocol

- a. Does the proposed research described in Study No. AHE34 from the Agricultural Handlers Exposure Task Force appear likely to generate scientifically reliable data, which will be useful, together with other data, for assessing the potential levels of pesticide exposure received by people when mixing, loading or applying a liquid pesticide with closed systems? [Note: In a few cases, corresponding application events are also to be monitored; the same question applies to those elements of the study.]
- b. Does the proposed research described in Study No. AHE34 from the Agricultural Handlers Exposure Task Force appear to comport with the applicable requirements of 40 CFR part 26, subparts K and L?

2. AHETF Airblast Application to Trellis Crops in the West Protocol

- a. Does the proposed research described in Study No. AHE36 from the Agricultural Handlers Exposure Task Force appear likely to generate scientifically reliable data, which will be useful, together with other data, for assessing the potential levels of pesticide exposure received by people when making an airblast application of a pesticide to a trellis crop under conditions found in the western United States? [Note: In a few cases, corresponding mixing/loading events are also to be monitored; the same question applies to those elements of the study.]
- b. Does the proposed research described in Study No. AHE36 from the Agricultural Handlers Exposure Task Force appear to comport with the applicable requirements of 40 CFR part 26, subparts K and L?

3. AHETF Airblast Application to Trellis Crops in the East Protocol

- a. Does the proposed research described in Study No. AHE37 from the Agricultural Handlers Exposure Task Force appear likely to generate scientifically reliable data, which will be useful, together with other data, for assessing the potential levels of pesticide exposure received by people when making an airblast application of a pesticide to a trellis crop under conditions found in the eastern United States? [Note: In a few cases, corresponding mixing/loading events are also to be monitored; the same question applies to those elements of the study.]
- b. Does the proposed research described in Study No. AHE37 from the Agricultural Handlers Exposure Task Force appear to comport with the applicable requirements of 40 CFR part 26, subparts K and L?

4. AHETF Closed Cab Airblast Application to Orchards Protocol

- a. Does the proposed research described in Study No. AHE38 from the Agricultural Handlers Exposure Task Force appear likely to generate scientifically reliable data, which will be useful, together with other data, for assessing the potential levels of pesticide exposure received by people when making an airblast application of a pesticide to orchard crops? [Note: In a few cases, corresponding mixing/loading events are also to be monitored; the same question applies to those elements of the study.]
- b. Does the proposed research described in Study No. AHE38 from the Agricultural Handlers Exposure Task Force appear to comport with the applicable requirements of 40 CFR part 26, subparts K and L?

5. *AHETF Fixed-Wing Aerial Application Protocol*

a. Does the proposed research described in Study No. AHE42 from the Agricultural Handlers Exposure Task Force appear likely to generate scientifically reliable data, which will be useful, together with other data, for assessing the potential levels of pesticide exposure received by people making an aerial application of a pesticide from fixed-wing aircraft?

[Note: In a few cases, corresponding mixing/loading events are also to be monitored; the same question applies to those elements of the study.]

b. Does the proposed research described in Study No. AHE42 from the Agricultural Handlers Exposure Task Force appear to comport with the applicable requirements of 40 CFR part 26, subparts K and L?