6/26/07 DRAFT

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
HUMAN STUDIES REVIEW BOARD (HSRB)
JUNE 27-29, 2007
PUBLIC MEETING

Wednesday, June 27, 2007
Environmental Protection Agency
Conference Center - Lobby Level
One Potomac Yard (South Bldg.)
2777 S. Crystal Drive
Arlington, VA 22202

HSRB WEB SITE http://www.epa.gov/osa/hsrb/
Docket Telephone: (202) 566 1752
Docket Number: EPA-HQ-ORD-2007-0403

BOARD REVIEW OF ITS DRAFT APRIL 18-20, 2007 HSRB MEETING REPORT, ORIGINALLY SCHEDULED AT THE BEGINNING OF THIS MEETING MAY BE RESCHEDULED EITHER LATER DURING THE MEETING OR AT A SUBSEQUENT TELECONFERENCE. IN ADDITION, TODAY'S MEETING MAY START EARLIER THAN LISTED ON THE AGENDA*

- **11:30 AM** **Convene Meeting and Identification of Board Members** – William Brimijoin, Ph.D. (HSRB Vice Chair)
- **11:40 AM** **Welcome –** George Gray, Ph.D. (EPA Science Advisor)
- **11:50 AM** **Opening Remarks –** Debbie Edwards, Ph.D. (Director, Office of Pesticide Programs, [OPP])
- **12:00 PM** **Meeting Administrative Procedures** - Paul Lewis, Ph.D. (Designated Federal Officer [DFO], HSRB, OSA, EPA)
- **12:05 PM** **EPA Follow-up on HSRB Recommendations –** Mr. William Jordan (EPA, OPP)

Carroll-Loye Picaridin Mosquito Repellency Protocol LNX-001

- **12:15 AM** **Science and Ethics of Carroll-Loye Protocol** –Mr. Kevin Sweeney (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **1:00 PM** **Lunch**
- **2:00 PM** **Public Comments**
- **2:30 PM** **Board Discussion**

a. If the proposed research described in Protocol LNX-001 from Carroll-Loye Biological Research is revised as suggested in EPA's review, does the research appear likely to generate scientifically reliable data, useful for assessing the efficacy of the test substances for repelling mosquitoes?

b. If the proposed research described in Protocol LNX-001 from Carroll-Loye Biological Research is revised as suggested in EPA's review, does the research appear to meet the applicable requirements of 40 CFR part 26, subparts K and L?

ICR Picaridin Mosquito Repellency Protocol

- **3:30 PM** **Science and Ethics of ICR Protocol** – Mr. Kevin Sweeney. (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **4:15 PM** **Public Comments**
- **4:45 PM** **Break**
- **5:15 PM** **Board Discussion**

a. If the proposed research described in ICR's proposed picaridin protocol is revised as suggested in EPA's review, does the research appear likely to generate scientifically reliable data, useful for assessing the efficacy of the test substances for repelling mosquitoes?

b. If the proposed research described in ICR's proposed picaridin protocol is revised as suggested in EPA's review, does the research appear to meet the applicable requirements of 40 CFR part 26, subparts K and L?

- **6:15 PM** **Adjournment**

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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Thursday, June 28, 2007
Environmental Protection Agency
Conference Center - Lobby Level
One Potomac Yard (South Bldg.)
2777 S. Crystal Drive
Arlington, VA 22202

- **8:30 AM** **Convene Meeting** – Steven Brimijoin, Ph.D. (HSRB Vice Chair)
- **8:40 AM** **Follow-up From Previous Day's Discussion –** Mr. William Jordan (OPP, EPA)

Acrolein

- **8:50 AM** **Acrolein** – Abdallah Khasawinah, Ph.D. (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **9:45 AM** **Public Comments**
- **10:15 AM** **Break**
- **10:30 AM** **Board Discussion**

a. The Agency has concluded that this study contains information sufficient for assessing human risk resulting from potential acute inhalation exposure. Please comment on whether the study is sufficiently sound, from a scientific perspective, to be used to estimate a safe level of acute inhalation exposure to acrolein.

b. Please comment on the following:

(1) Is there clear and convincing evidence that the conduct of the study was fundamentally unethical?

(2) 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?

4-Amino Pyridine

- **11:30 AM** **4-Amino Pyridine** – Abdallah Khasawinah, Ph.D. (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **12:15 PM** **Public Comments**
- **12:30 PM** **Lunch**
- **1:30 PM** **Board Discussion**

a.The Agency's weight-of-evidence (WOE) document for 4-aminopyridine describes the study design and results of three clinical trials (**Grijalva et al. 2003, Segal et al. 1999, and Van Diemen et al. 1993)**. The WOE document also discusses the Agency's conclusion that these studies provide sufficient information to establish a point of departure for the assessment of the

risk to humans resulting from all potential durations of exposure to 4-AP. Please comment on whether the studies are sufficiently sound, from a scientific perspective, to be used to derive a point of departure for estimating risk to humans from exposure to 4-AP.

b. Please comment on the following:

(1) Is there clear and convincing evidence that the conduct of any of the clinical studies was fundamentally unethical?

(2) Is there clear and convincing evidence that the conduct of any of the clinical studies was significantly deficient relative to the ethical standards prevailing at the time the research was conducted?

- **2:30 PM Break**

AEATF and AHETF Research Programs

Introduction

- **2:45 PM EPA Presentation** - William Jordan (EPA, OPP)

Overview / Risks and Benefits of Handler Research

- **2:50 PM EPA Presentation – Mr**. John Carley (OPP, EPA)
- **3:30 PM Public Comments**
- **3:45 PM Board Discussion**

Risks and Benefits of Handler Research

1). Will the Task Forces' Governing Documents considered in conjunction with the additional study- and scenario-specific information specified above provide an adequate basis for assessing whether the risks of conducting a particular study are justified by the expected benefits of the proposed research? If not, what additional information should be provided for an IRB, EPA, and the HSRB?

Addressing Potential Sources of Underestimation Bias/QA and QC Controls

- **5:00 PM EPA Presentation –** Mr. Jeff Dawson (OPP, EPA)
- **5:30 PM Public Comments**
- **5:45 PM Adjournment**

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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Friday, June 29, 2007
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Conference Center - Lobby Level
One Potomac Yard (South Bldg.)
2777 S. Crystal Drive
Arlington, VA 22202

- **8:30 AM** **Convene Meeting** – Steven Brimijoin, Ph.D. (HSRB Vice Chair)
- **8:40 AM** **Follow-up From Previous Day's Discussion –** Mr. William Jordan (OPP, EPA)

AEATF and AHETF Research Programs:

Addressing Potential Sources of Underestimation Bias; QA and QC Controls (continued)

- **8:50 AM** **Board Discussion**

Addressing Potential Sources of Underestimation Bias

1) Has EPA appropriately characterized the limitations on the scientific usefulness of a handler database that does not include data characterizing the efficiency of residue removal procedures? If not, what limitations have been overlooked?

2) Has EPA identified the relevant scientific and practical considerations affecting the choice to include biomonitoring, and has EPA appropriately characterized the limitations on the scientific usefulness of the resulting data if no biomonitoring is conducted? If not, what other considerations should bear on a decision to conduct biomonitoring in addition to WBD?

QA/QC Controls

1) Do the Task Forces' Standard Operating Procedures appear adequate to ensure that the data resulting from the proposed research will be of high quality? If not, what other Quality Assurance or Quality Control procedures need to be addressed?

- **10:00 AM** **Break**

Design of Scenario-Level Sampling; Statistical Justification of Number of Clusters; and Monitoring Units and Within Worker Variability

- **10:15 AM** **EPA Presentation** – Mr. David Miller (OPP, EPA)
- **11:00 AM** **Public Comments**

• **11:15 AM Board Discussion**

Design of Scenario-Level Sampling

With regard to the AHETF and AEATF plans to conduct their proposed handler research using purposive diversity sampling strategies:

1) Has EPA identified the relevant scientific and practical considerations affecting the choice of a strategy for sample selection? If not, what other considerations should bear on the choice?

2) Does the HSRB agree with EPA that the Task Forces should provide scenario-specific information about the availability of data to identify significant variables (other than AaiH) potentially influencing exposure and about the feasibility of developing a sampling strategy to address those variables quantitatively? If not, what additional information is needed?

3) Has EPA appropriately characterized the limitations on the scientific usefulness of the resulting data attributable to the choice of the sampling strategy? If not, what has EPA overlooked?

Statistical Justification of Number of Clusters

1. What additional information, if any, would the HSRB need to assess the adequacy of the justification for the number of clusters and number of MUs in specific AHETF and AEATF study proposals?

Within-Worker Variability

1. Has EPA appropriately characterized the limitations on the scientific usefulness of a database that does not include repeated measures? If not, what limitations has EPA overlooked?

• **12:15 PM Lunch**

Subject Recruitment and Enrollment Issues

• **1:15 PM EPA Presentation -** Mr. John Carley (OPP, EPA)
• **1:45 PM Public Comments**
• **2:00 PM Board Discussion**

1. Does the Board agree that the Governing Documents and associated SOPs of the AHETF and AEATF research programs include comprehensive and appropriate protections for human subjects of the research? If not, what has been overlooked?

2. In singling out the handling of language differences as an area requiring further refinement, has EPA overlooked other areas in need of revision? If so, what?

- **3:00 PM** **Adjournment -** Steven Brimijoin, Ph.D. (HSRB Vice Chair) and Paul Lewis, Ph.D. (DFO, HSRB, OSA, EPA)

* Please be advised that agenda times are approximate and subject to change. For further information, please contact the Designated Federal Officer for this meeting, Paul Lewis via telephone: (202) 564-8381 or email: lewis.paul@epa.gov