10/22/07 DRAFT

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
HUMAN STUDIES REVIEW BOARD (HSRB)
OCTOBER 24-26, 2007
PUBLIC MEETING

Wednesday, October 24, 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-2007-0942

- **8:30 AM** **Convene Meeting and Identification of Board Members** – Celia Fisher, Ph.D. (HSRB Chair)
- **8:40 AM** **Welcome –** George Gray, Ph.D. (EPA Science Advisor)
- **8:45 AM** **Opening Remarks –** Debbie Edwards, Ph.D. (Director, Office of Pesticide Programs, [OPP])
- **8:50 AM** **Meeting Administrative Procedures** - Paul Lewis, Ph.D. (Designated Federal Officer [DFO], HSRB, OSA, EPA)
- **8:55 AM** **EPA Follow-up on HSRB Recommendations –** Mr. William Jordan (EPA, OPP)

Scientific and Ethical Approaches for Observational Exposure Studies

- **9:05 AM** **EPA Draft Document *Scientific and Ethical Approaches for Observational Exposure Studies*–** Roy Fortmann, Ph.D. and Larry Cupitt, Ph.D. (Office of Research and Development, EPA)
- **10:15 AM** **Break**
- **10:30 AM** **Public Comments**
- **11:00 AM** **Board Discussion**

One of the goals of the document is identify the major scientific and ethical areas and issues that researchers should address in the design and implementation of observational human exposure measurement studies, with the emphasis on the areas requiring ethical considerations. Does each section identify the major areas and issues where ethical considerations should be addressed?

- **12:15 PM** **Lunch**
- **1:00 PM** **Board Discussion (continued)**

The document is intended to serve as a reference and resource of information that researchers can use in the design and implementation of observational exposure studies. Are there additional sources of information that should be considered for inclusion in the section?

Is the information presented accurately and clearly in each section?

Note: Board discussion will focus on responding to the three charge questions together by section (Sections 1 to 7) of the EPA draft document

Sodium Azide

- **1:45 PM** **Science and Ethics of Sodium Azide Study** – Ms. Nancy McCarroll (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **2:30 PM** **Public Comments**
- **2:45 PM** **Board Discussion**

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

Please comment on the following:

> Is there clear and convincing evidence that the conduct of the study was fundamentally unethical?
>
> 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?

- **3:30 PM** **Adjournment**

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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PUBLIC MEETING
Thursday, October 25, 2007
Environmental Protection Agency
Conference Center - Lobby Level
One Potomac Yard (South Bldg.)
2777 S. Crystal Drive
Arlington, VA 22202

- **8:00 AM** **Convene Meeting** – Celia Fisher, Ph.D. (HSRB Chair)
- **8:05 AM** **Follow-up From Previous Day's Discussion –** Mr. William Jordan (OPP, EPA)

Science Issues in Mosquito Repellent Efficacy Field Research

- **8:10 AM** **Introduction –** Celia Fisher, Ph.D. (HSRB Chair)
- **8:20 AM** **EPA Presentation -** Mr. William Jordan (EPA, OPP)
- **8:40 AM** **Public Comments**
- **8:55 AM** **Board Discussion**

Issue 1.

- What do data show about the variability of the time intervals between first and subsequent landings in mosquito repellent field trials?

- What is the current scientific understanding of how factors other than repellent efficacy could affect the likelihood that an initial event—a mosquito landing or mosquito bite—would be "confirmed" by another similar event within 30 minutes? Please address at least these factors:

  - Characteristics of mosquito populations
  - Characteristics of test sites
  - Characteristics of test subjects
  - Characteristics of test methods

- Can the impact of such factors on the likelihood or timing of an initial and confirming event be predicted? Can it be quantified?

Issue 2.

At its June 27 - 29, 2007 meeting the Board learned that different designs with different "length-biased" sampling for mosquito repellent field studies are in use. One design exposes subjects to potential mosquito landings for one minute of every 15 minutes; another design exposes subjects to potential mosquito landings for five minutes of every 30 minutes. The DFO is separately providing a CD containing the background materials for the June 27 – 29, 2007 HSRB meeting. The protocols are loaded on the CD. These designs have different "length-biased" sampling.

- What is the methodological rationale for the two different designs?

- Which design is used more widely in the field? Why?

- Can potential effects of variation in the pattern of intermittent exposure on the results of efficacy testing be isolated from the effects of other variables? If so, can the direction or magnitude of the effects be predicted? How might these influences be analyzed and accounted for in collecting, reporting and analyzing repellent efficacy data?

Issue 3.

Dr. Matt Kramer, a USDA statistician who has served as a consultant, has suggested that the precision of estimates of Complete Protection Time (CPT) in repellent testing could be significantly increased by defining a failure of efficacy as the mean time from treatment to a series of several landings or bites. He has stated:

> The precision of CPT increases when it is estimated beyond time to [First Confirmed Bite] FCB or FCLanding. How well CPT can be estimated depends on the distribution of so many bites beyond FCB. The number of mosquitoes that will bite (*n*) will determine results of the test. Each person in the field should be his/her own control; that way it is possible to know *n* per person, and reduce person-to-person variability.
>
> If using the mean time to the first 5 bites, the SE will decrease proportionally as *n* increases ($n = 5$ in this case). That is equivalent to an increase in the power of the test of 5 times. This method allows for detecting formulation differences near the CPT.

- Does this approach, indeed, increase the precision of estimates of CPT markedly without requiring additional subjects?

- If so, would this increased precision justify the incremental risk to the subjects resulting from their exposure to a greater number of mosquito landings?

- Is it practical to test long-lasting repellents to the point of five landings?

- **10:00 AM Break**
- **10:15 AM Board Discussion (continued)**

Completed Field Efficacy Studies by Carroll-Loye Biological Research: SCI-001 and WPC-001

- **11:15 AM EPA Science and Ethics of Completed Carroll-Loye Biological Research Studies SCI-001 and WPC-001** – Clara Fuentes, Ph..D. (OPP, EPA), Mr. Kevin Sweeney (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **12:15 PM Lunch**

- **1:15 PM Public Comments**
- **1:45 PM Board Discussion**

SCI-001

Is this study sufficiently sound, from a scientific perspective, to be used to assess the repellent efficacy of the formulations tested against mosquitoes? Please comment specifically on:

> Whether participation in field testing by several subjects on the day after they had been treated with a different test repellent is likely to have affected the validity of the results for those subjects on those days.
>
> The effects of changes to the experimental design resulting in evaluation of repellents using fewer than ten subjects per treatment per day, followed by pooling of results by site for statistical analysis.

Does available information support a determination that this study was conducted in substantial compliance with subparts K and L of EPA regulations at 40 CFR part 26? Please comment specifically on:

> The decision to use a different test formulation in place of one of the test materials described in the protocol reviewed by the IRB, EPA and the HSRB.
>
> How to assess the ethical conduct of an insect repellency study involving multiple test formulations when there is an ethical deficiency in the conduct of the study with respect to one of the test formulations. If the ethical deficiency warrants not relying on the results of the testing with regard to one test formulation, under what circumstances (if any) does the ethical deficiency affect the acceptability of the results from testing the other formulations?

WPC-001

Is the research conducted under WPC-001 sufficiently sound, from a scientific perspective, to be used to assess the repellent efficacy of the formulation tested against mosquitoes? Please comment specifically on whether participation in field testing by several subjects on the day after they had been treated with a different test repellent is likely to have affected the validity of the results for those subjects on those days.

Does available information support a determination that the research covered by WPC-001 was conducted in substantial compliance with subparts K and L of EPA regulations at 40 CFR part 26? If the conduct of any part of SCI-001 is deemed not to substantially comply with the requirements of subparts K and L, please comment specifically on how to assess the ethical conduct of research conducted under WPC-001 in light of the fact that it was conducted at the same times and at the same places as the research covered under protocol SCI-001.

- **3:00 PM Break**

Carroll-Loye Biological Research Insect Repellent Efficacy Protocols
SPC-001

- **3:15 PM Science and Ethics of Carroll-Loye Protocol SPC-001** – Mr. Kevin Sweeney (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **3:45 PM Public Comments**
- **4:00 PM Board Discussion**

If the proposed research described in Protocol SPC-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?

If the proposed research described in Protocol SPC-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?

SPC-002

- **5:00 PM Science and Ethics of Carroll-Loye Protocol SPC-002** – Mr. Kevin Sweeney (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **5:30 PM Public Comments**
- **5:45 PM Board Discussion**

If the proposed research described in Protocol SPC-002 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?

If the proposed research described in Protocol SPC-002 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?

- **6:45 PM Adjournment**

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Friday, October 26, 2007
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- **8:30 AM** **Convene Meeting** – Celia Fisher, Ph.D. (HSRB Chair)
- **8:35 AM** **Follow-up From Previous Day's Discussion –** Mr. William Jordan (OPP, EPA)

ICR Repellency Efficacy Protocol A117

- **8:40 AM** **EPA Science and Ethics Reviews of ICR Protocol A117**– Mr. Kevin Sweeney (OPP, EPA) and Mr. John Carley (OPP, EPA)
- **9:15 AM** **Public Comments**
- **9:30 AM** **Board Discussion**

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 of the genus *Culex*?

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?

- **10:30 AM** **Break**

EPA Update of AEATF and AHETF Research Programs

- **10:45 AM** **EPA Presentation -** William Jordan (OPP, EPA)
- **11:00 AM** **Public Comments**
- **11:15 AM** **Board Discussion**

No Board Charge

- **12:30 PM** **Adjournment -** Celia Fisher, Ph.D. (HSRB 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