April 14, 2006

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
HUMAN STUDIES REVIEW BOARD (HSRB)
May 2 – 4, 2006
PUBLIC MEETING

Holiday Inn Hotel and Suites
Alexandria – Historic District
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Docket Telephone: (202) 566 1752
Docket Number: EPA-HQ-ORD-2006-0310

CHARGE TO THE BOARD

Part 1. Chromium

Hexavalent chromium is a component of a pesticide product intended to be used as a wood preservative. Members of the general public may experience dermal exposure to residues of hexavalent chromium remaining on wood treated with a wood preservative. Because chromium has caused allergic contact dermatitis (ACD) in occupational settings, EPA has determined that it should assess the potential for ACD in the general public resulting from the use of wood preservatives containing chromium.

In a meeting of the FIFRA Scientific Advisory Panel (SAP) in May 2004, EPA obtained independent peer review of scientific issues related to the assessment of the potential dermal risk resulting from exposure to chromium. See www.epa.gov/scipoly/sap/2004/final.doc The Agency has carefully considered the report of the SAP, as well as the advice of EPA scientists through the steering committee of the Agency's Science Policy Council. Taking all of this into account, EPA has derived a "sensitization reference dose" (RfD) based on the 10% Minimum Elicitation Threshold (MET 10) and use of a 10-fold uncertainty factor for potential variability within the human population and other uncertainties. See ADTAC Memorandum, "***Hexavalent Chromium*** - Finalization of Issues related to Quantitation of Dermal Risk from exposure to treated wood containing hexavalent chromium," August 31, 2004.

1. Scientific considerations:

EPA has identified a study performed with subjects who had documented sensitivity to chromium (Nethercott, et al., 1994). The study was conducted to identify a level of exposure to chromium below which dermal exposure did not appear to elicit an ACD response. Regarding the Nethercott human study, the

Agency has concluded that the study contains information sufficient for assessing human risk resulting from potential dermal exposure.

Please comment on whether the Nethercott study is sufficiently sound, from a scientific perspective, to be used to estimate a safe level of dermal exposure to hexavalent chromium.

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 Nethercott 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 2. Carbofuran

Carbofuran is an *N*-methyl carbamate (NMC) pesticide whose primary toxic effect is neurotoxicity caused by the inhibition of the enzyme, acetylcholinesterase, via carbamylation followed by rapid recovery. Carbofuran can, at sufficiently high doses, lead to a variety of clinical signs. The Agency is conducting acute, aggregate (single chemical, multi-route) and worker risk assessments of carbofuran. In addition, carbofuran is a member of the *N*-methyl carbamate common mechanism group and is thus included in the cumulative (multi-chemical, multi-route) risk assessment for the NMCs.

1. Scientific considerations:

The Agency's WOE document and DERs for carbofuran describe the study design and results of a carbofuran human oral study and two human dermal toxicity studies. The WOE document also discusses the Agency's conclusions that these studies are useful in establishing points of departure, both oral and dermal, for the single chemical assessment and in informing the interspecies uncertainty factor for the cumulative assessment.

Please comment on the scientific evidence that supports these conclusions.

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 any of the human studies conducted with carbofuran was fundamentally unethical?

b. Is there clear and convincing evidence that the conduct of the studies was significantly deficient relative to the ethical standards prevailing at the time the research was conducted?

Part 3. Methyl Isothiocyanate (MITC)

MITC is an irritating compound that has a limited animal database for toxicity via inhalation, the key route of exposure. MITC can be used as a pesticide directly to treat wood poles, but the major pathway of exposure to MITC is from degradation of several fumigant pesticides (i.e., metam sodium, metam potassium, and dazomet). Due to its volatility, MITC has the potential to move off-site, which can result in exposure to bystanders near treated areas and, through ambient air, to people far away from treated areas. Use of the soil fumigants also results in exposure to those handling the pesticides or working in treated fields.

1. *Scientific considerations:*

The Agency's WOE document and DER for MITC describe the study design and results of the MITC odor threshold and eye irritation human studies. The WOE document also discusses the Agency's conclusions that the eye irritation study is useful for the assessment of potential effects on bystanders and workers from exposures to MITC during acute (1-day) intervals. The Agency has concluded that the odor threshold study is less useful than the eye irritation study for assessing the human health effects of MITC, since the odor detection threshold for humans is higher than the level that causes eye irritation. The Agency has decided, however, to use the results of the eye irritation study for assessing the inhalation exposure of MITC.

Please comment on the scientific evidence that supports this conclusion.

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 human eye irritation study with MITC was fundamentally unethical?

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