UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

Memorandum

DATE: December 13, 2006

SUBJECT: Transmission of Background Materials and Charge to the Panel for the January 9-12, 2007 Session of the FIFRA Scientific Advisory Panel (SAP) Entitled "Review of Worker Exposure Assessment Methods"

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Attached are 30 compact discs and 2 paper copies of all background documents and the charge to the panel for the January 9-12, 2007 FIFRA SAP session. These materials do not contain any information protected under statute as Confidential Business Information (CBI). These materials do contain information protected from disclosure to foreign and multi-national pesticide producers under FIFRA Section 10(g). In addition, these materials include information protected by copyright. The attached documents and/or electronic files include the following:

Document Title	Author(s)	Date	Indicate Whether FIFRA 10(g) or © Protected
Transmission of Background Materials and Charge to the Panel for the January 9-12, 2007 Session of the FIFRA Scientific Advisory Panel (SAP) Entitled "Review of Worker Exposure Assessment Methods"	Jeff Evans	12/13/06	
Review of Worker Exposure Assessment Methods	U.S. EPA *et al.*	12/13/06	
Excel Spreadsheet With Filename: ExhibitA.PHEDCaseStudy.v102006	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitB.HandMethodsAnalysisPtA.102306	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitB.HandMethodsAnalysisPtB.110106	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_I_a_ML_DF_RawData.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_I_b_ML_DF_outer.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_I_c_ML_DF_inner.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_II_a_L_Gran_RawData.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_II_b_L_Gran_outer.xls	U.S. EPA	12/13/06	

Excel Spreadsheet With Filename: ExhibitC_II_c_L_Gran_inner.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_III_a_ML_Liq_RawData.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_III_b_ML_Liq_outer.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_III_c_ML_Liq_inner.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_IV_a_APP_Open-CabAirblast_RawData.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_IV_b_APP_Open-CabAirblast_outer.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_IV_c_APP_Open-CabAirblast_inner.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_V_a_APP_Closed-CabAirblast_RawData.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_V_b_APP_Closed-CabAirblast_outer.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_V_c_APP_Closed-CabAirblast_inner.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_VI_a_APP_Open-CabSolidSpreader_RawData.xls	U.S. EPA	12/13/06	
Excel Spreadsheet With Filename: ExhibitC_VI_c_APP_Open-CabSolidSpreader_inner.xls	U.S. EPA	12/13/06	
Agricultural Handlers Exposure Task Force (AHETF) Technical Summary Document For a Multi-Year Pesticide Handler Worker Exposure Monitoring Program	AHETF	12/06/06	
The Conservative Nature of the Current Practice in Estimating Pesticide Handler and Reentry Dermal Exposures and Doses	AHETF	12/07/06	
Passive Dosimetry Data Derived from the Outdoor Residential Exposure Task Force & Pesticide Handler Exposure Databases - Comparisons to Biomonitoring Data (Sponsor: AHETF & ORETF)	AHETF	12/07/06	
Summary Comparative Evaluation of Absorbed Dose Estimates Derived From Passive Dosimetry Measurements With Those Derived From Biological Monitoring : Validation of Exposure Monitoring Methodologies (Sponsor AHETF)	AHETF	12/07/06	
Procedures for Determining the Required Number of Clusters and Monitoring Units per Cluster to Achieve Benchmark Adequacy	AHETF	12/07/06	
Comparative Evaluation of Absorbed Dose Estimates Derived From Passive Dosimetry Measurements With Those Derived From Biological Monitoring : Validation of Exposure Monitoring Methodologies (Sponsor AHETF)	AHETF	12/08/06	
AEATF II Background and Scoping Summary	AEATF	11/28/06	
Data Review and Study Acceptance Criteria: For Inclusion of Existing Antimicrobial Exposure Monitoring Studies in the Antimicrobial Exposure Assessment Task Force II (AEATFII) Database	AEATF	11/28/06	
Glossary of Terms	AEATF	11/28/06	

Charge to the Panel: January 9-12, 2007 FIFRA Scientific Advisory Panel

EPA has prepared a document, dated December 12, 2006, that contains the Agency's technical review of worker exposure methods. This memo contains the questions and issues posed by EPA to the panel for discussion. In addition to this memo, several documents/files are provided as supporting information.

I. Overview of EPA's Approach to Estimating Handler Exposure

The Agency defines individuals involved in pesticide applications as handlers. Handler tasks (e.g., aerial application of pesticides) are routinely evaluated in exposure assessments using dermal and inhalation variables referred to as unit exposures. Unit exposures are normalized values calculated from handler exposure studies described in the 1986 Pesticide Assessment Guidelines, Subdivision U – Applicator Exposure Monitoring (currently referred to as Series 875, Group A). A unit exposure (mg/lb active ingredient) is calculated by dividing the pesticide residues (mg) measured using dosimetry, worn by a volunteer performing a certain handler activity (scenario) by the number of pounds of pesticide active ingredient (ai) used by that volunteer. In exposure assessments, scenario-specific unit exposures are multiplied by estimates of the amount of ai handled for a given handler scenario (e.g., number of pounds ai sprayed to wheat per day for an aerial applicator). These simple calculations are daily exposure estimates (mg/day) which can then be adjusted by body weight (kg) and dermal absorption if necessary. The resulting metric (mg/kg/day) is then compared to doses from toxicity studies (mg/kg/day) in Agency risk assessments.

A. The PHED database

The Agency relies on the Pesticide Handlers Exposure Database (PHED) as a source of generic unit exposure estimates. PHED was designed by a task force of representatives from the U.S. EPA, Health Canada, the California Department of Pesticide Regulation, and member companies of the American Crop Protection Association. PHED is a software system consisting of two parts -- a database of measured exposure values for workers involved in the handling of pesticides under actual field conditions and a set of computer algorithms used to segment and statistically summarize the selected data. Currently, the database contains values for over 1,700 individual monitoring events (i.e., monitoring units). Once the data for a given exposure scenario have been selected, the data are typically normalized (i.e., divided) by the amount of pesticide handled resulting in standard unit exposures. Following normalization, the data are statistically summarized. The distribution of exposure values for each body part (e.g., chest, upper arm) is categorized as normal, lognormal, or "other" (i.e., neither normal nor lognormal). A central tendency value is then selected from the distribution of the exposure values for each body part. These values are the arithmetic mean for normal distributions, the geometric mean for lognormal distributions, and the median for all "other" distributions. Once selected, the central tendency values for each body part are summed to define the exposure for the entire body

The data in PHED are based on the use of passive dosimetry methods (e.g., patches, gloves, wholebody dosimeters or washes) to estimate the magnitude of, and patterns of exposure resulting from various handling activities. Knowledge of exposure patterns by body part is critical for risk managers making exposure mitigation decisions. For example, EPA may require chemical resistant gloves if exposure is primarily to the hands.

One of the fundamental limitations of PHED is the data come from multiple study designs. PHED contains studies that were conducted from 1977 to 1994. Prior to the development of the Subdivision U guidelines, investigators limited the collection of measurements to areas of the body they believed to have the greatest potential for exposure. After the guidelines were established in 1986, measurements representing the head, neck, chest, back, arms, legs and hands were more routinely collected. Consequently in PHED, a unit exposure for a given scenario has the potential for a different number of observations and distribution per body part when their central values are summed for a total body estimate as described above. For example a unit exposure for a given scenario could include studies in which only the hands were measured; plus studies in which only the hands and forearms were measured, and so on.

The material and methods of collecting residues from volunteers participating in handler studies have evolved over time, and these competing study designs have a confounding effect on PHED outputs. Like the studies with differing body part measurements, the studies in the database for a given scenario could also be based on studies having differing dosimetry methods (e.g., patches or whole body dosimeters). These methods are described in the background document. One of the primary concerns regarding competing monitoring methods is the putative differences in the performance of cotton gloves and hand rinses used to collect pesticide residues from hands. A fundamental question is: do estimates of exposure based on using cotton gloves as dosimeters overestimate hand measurements? Conversely; do estimates of exposure based on hand rinses underestimate hand measurements?

The Agency has investigated the performance of various techniques for measuring hand exposure and other biases of passive dosimetry for underestimating exposure in a number of ways. First, a review of available peer reviewed literature on the subject of hand rinses was conducted. Second, an analysis was performed comparing hand measurements made with varying techniques based on data available in PHED. Third, comparisons were made of estimates of exposure made with passive dosimetry and a more chemical-specific method - measuring internal metabolites of pesticides in urine referred to as biological monitoring.

B. Exploring the Relationship of Handler Exposure to Amount of Pesticide Handled

Since the establishment of the guidelines, the Agency has assumed that the magnitude of exposure is proportional to the amount of active ingredient handled (AaiH) and, that scenario and activity are independent variables. In a regulatory setting, the assumption of proportionality is useful because it enables risk managers to mitigate risk by reducing labeled application rates if mitigation involving Personal Protective Equipment or engineering controls continue to indicate risks of concern.

EPA analyzed and examined PHED data for six different handler scenarios with respect to the relationship between AaiH and exposure. Improving our understanding of this phenomenon with the available data in PHED will help the Agency 1) to determine the need for additional data and 2) gain insight when evaluating data to populate a new database. The AHETF is proposing as part of its future studies to investigate proportionality as a secondary objective of its study protocols. They intend to incorporate more advanced statistical concepts and designs in their analysis to distinguish between complete proportionality and complete independence of exposure and AaiH. An important document to consider is the AHETF document: Procedures for Determining the Required Number of Clusters and Monitoring Units per Cluster to Achieve Benchmark Adequacy.

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C. EPA Exposure Assessments (EA)

EPA currently conducts deterministic risk assessments by relying on central tendency PHED unit exposures coupled with high-end label use rates and work hours for each relevant handler scenario

/activity. As the tools and techniques for performing probabilistic assessments improve, the limitations of PHED become more apparent. Chief among them is the inability to construct individual full body exposure estimates and develop ranges and distributions of AaiH.

II. Development of an Improved Approach

A. PHED database limitations

PHED has been a valuable scientific and regulatory tool but has several limitations. These include scenarios consisting of values taken from studies having multiple study designs, compositing varying numbers of body parts in a given unit exposure, and the inability to evaluate inter- and intra- personal variability since varying numbers of individuals were used in the sample collection process. PHED has limited (and in some cases is lacking) studies representing advances in agricultural equipment, pesticide formulations and application techniques.

B. EPA desire to have more refined Exposure Assessments

The Agency envisions the next generation handler database to be one that can be used to describe more fully the range of potential handler exposures and that can produce inputs for use in probabilistic exposure assessments. We recognize that improvements in pesticide use information (i.e., the amount of active ingredient handled) will also need to be made. However, until those advances are made, we believe it is desirable to have scenario specific values that can be used to develop distributions representing the advances made in pesticide application equipment and techniques.

C. Criticisms from stakeholders

Our exposure assessments generate a number of criticisms from important stakeholders that the Agency would like to address. Some of the criticisms include the use of central tendency values, the potential for certain passive dosimetry techniques to underestimate exposure, and that the studies are based on activities involving outdated equipment. Ideally a new database would consist of handler scenarios that would have sufficient samples representative of as many monitoring activities performed by as many different individuals and at as many different locations as possible. It is also important that the samples be collected in as consistent a manner as possible such that confounding by the use of multiple methods is minimized.

D. Human Subject Review Board review

In June 2006, the AHETF submitted five protocols for field trials for an ethics review by the Human Subjects Review Board (HSRB) pursuant to 40 CFR 26, subpart K. The protocols described five field trials that were part of their 2006 data collection efforts. These trials are part of multi-year effort to develop data to populate the Agricultural Handlers Exposure Database (AHED). In their review, the HSRB identified many issues relating to dermal exposure collection methods selected by the AHETF and noted that they did not adequately indicate how their sample size was derived. In addition, they asserted that the Agency had not articulated the need for these data with respect to its current database PHED. Consequently, the HSRB were unable to evaluate the ethical merits of the AHETF protocols since key scientific issues were not addressed. The report for this meeting of the HSRB can be found at http://www.epa.gov/osa/hsrb/files/june2006mtgreportfinal100606.pdf. Since the HSRB identified key scientific issues impacting many data generating efforts such as the AHETF and Antimicrobial Exposure Assessment Task Force (AEATF), the Agency believes the timing is appropriate for a scientific review of the methods and data analysis approaches that are to be used for the next generation of exposure data.

III. Charge questions

1) Data Needs

EPA believes that many studies within our current database have limitations. In some cases, the Agency is lacking data to address modern pesticide application equipment and techniques. EPA believes that additional data could significantly improve our ability to estimate and better characterize the range of worker exposure with greater certainty.

Please comment on these limitations and EPA's conclusion that additional data could improve significantly the Agency's ability to assess worker exposure. Also, please comment on the selection criteria proposed by the AHETF and AEATF in their respective submissions for evaluating the extent to which existing data would meet EPA's exposure assessment needs.

2) Passive Dosimetry Performance

The common approach for conducting dermal exposure monitoring studies relies on the use of whole-body dosimetry, handwashing, and facial/neck wipes. In some cases, biological monitoring is also used as an alternative method. Exposure estimates in Agency risk assessments; however, typically rely on "to the skin" measurements (i.e., potential dose) coupled with dermal absorption data or dermal toxicity studies in order to calculate risks. The Agency believes that these methods are complimentary and that they can provide appropriate estimates for exposure assessment but that the results directly relate to the reliability of the inputs used. Please comment on the Agency's conclusion regarding passive dosimetry and biological monitoring, including whether a systematic bias exists in either approach.

Based on the information presented, the Agency has particular concerns over three specific aspects of how these studies are conducted including (1) the possible need to correct for the efficiency of the handwashing technique; (2) compensating for absorption of residues through the skin during sample collection periods; and (3) the breakthrough of residues under whole-body dosimeter garments. Please comment on the need to systematically account for residue losses due to these potential method biases. If there is a need, please describe how these corrections should be accomplished in a way that could reduce uncertainties in the resulting exposure estimates.

3) Passive Dosimetry vs. Biomonitoring

EPA believes that a comparison of exposure estimates derived from data collected biomonitoring with data collected through passive dosimetry is the most appropriate way to assess the predictive nature of a passive dosimetry-based approach for estimating worker exposure. Please comment on the strengths and limitations of this kind of comparison for judging the potential utility of passive dosimetry data in conducting exposure assessments.

EPA has conducted such a comparison using available data and believes that the comparison shows sufficient concordance of estimates based on biomonitoring data and passive dosimetry data to support the conclusion that a passive dosimetry-based approach can generate data that can be used to develop relatively predictive estimates of worker exposure for a wide variety of scenarios and activities. Please comment on the adequacy of the analysis to support EPA's conclusion.

4) Normalization of Exposure by Amount of Active Ingredient Handled (AaiH)

The normalization of exposure by AaiH - the unit exposure - has, since the mid-1980s, been the principle relationship underlying the use of exposure data in the Agency's pesticide handler exposure assessments. It is based on the assumption that the two variables are proportional. That is, if one doubles the amount of pesticide they handled or applied, the resultant exposure will be doubled as well.

The Agency is unsure whether the results of our exploratory work showing that proportionality between exposure and AaiH is reasonable in some but not all cases, is a function of limitations of the data within PHED or whether this relationship is in fact not a reasonable assumption for all scenarios. It may be the case that an additional ancillary variable (e.g., boom length, # of tank mixes, or # de-couplings in a closed loading system), in addition to or in place of AaiH, may improve the predictive capabilities of our exposure model.

Though it is recognized that neither the studies in our current database nor the proposed studies by the AHETF were designed for the primary purpose of examining proportionality between exposure and AaiH or to determine the extent to which other parameters influence exposure, compared with our current database, the Agency believes that the proposed AHETF studies will generate data that will reinforce the assumption of proportionality between exposure and AaiH or, alternatively, inform the applicability of another variable as a more appropriate predictor of exposure.

Based on the themes presented on this topic including its historical precedent, its application in risk assessment and subsequent risk management decisions, the Agency's exploratory work using the six PHED scenarios in the case study, and the study design and objectives of the AHETF, please comment on the assumption of proportionality between exposure and AaiH, as a default. Also, please provide comments on whether the proposed AHETF study design is adequate to evaluate proportionality between exposure and AaiH? What other parameters should AHETF study designs measure in order to improve the prediction capabilities of our exposure model?

5) Within-worker and Between-worker Variability

The proposed AHETF study design does not include true worker replicates and is not intended to examine the issue of variability within workers. The AHETF notes that to appropriately investigate this issue would require significantly more sampling and resources. They propose, however, that their single-day exposure distribution results can be used to evaluate longer term multiple day exposures by placing reasonable limits on expected intra-class correlation coefficients (ICC): they indicate that, from their own research and review of the literature, the ICC is likely to be between 0.3 and 0.5 over relatively short periods of time (e.g., seasonal), and likely to be even lower over longer periods of time.

Please comment on the AHETF's approach to estimating the number of samples (MU) needed to determine within worker variability and their conclusion on the importance of measuring such variability in their proposed studies.

6) Sample Size: Number of Sites and Subjects per Scenario/Activity

The Agency's goal is to ensure that monitoring studies rely on sample sizes that adequately represent the range of exposure of people who engage in a particular handler scenario and activity. It is also recognized that occupational monitoring studies are costly and have many logistical obstacles. The Agency is also concerned about limiting the numbers of participants in these types of studies in accordance with the ethical requirements described in Subpart K (40CFR26) and the recent criteria outlined by the Agency's Human Studies Review Board. The Agency's current guidelines recommend 15 monitoring units for each scenario. In addition, the AHETF has provided a rationale for the number of

samples in their study design.

Please comment on the uncertainties associated with the Agency's and AHETF's recommended number of monitoring units. In your comments, please include any recommendations you may have regarding specific statistical analyses that may assist the Agency in developing better understanding of these uncertainties and characterizing them in a complete and transparent manner in Agency assessments based on these data.