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January 17, 2008 HSRB Work Group Teleconference on AHETF and AEATF Protocols Chair's Summary

Participants

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Work Group Goals

The HSRB Workgroup [Workgroup] was convened by teleconference to discuss HSRB concerns about the sampling designs proposed by the Agricultural Handler Exposure Task Force (AHETF) and the Antimicrobial Exposure Assessment Task Force (AEATF) [TFs] for their respective pesticide handler exposure monitoring programs. The Workgroup reviewed materials provided by the EPA Office of Pesticide Programs (OPP) in preparation for the April 2008 HSRB meeting. OPP anticipates presenting at least two AEATF protocols for HSRB review at the April meeting. The Summary of EPA/OPP Teleconferences with AHETF submitted by William Jordan was the primary focus of the conference call. The Workgroup members appreciated the detailed information and summary provided by OPP. It was clear from the summary and materials that OPP has carefully considered and in most instances supported all of the HSRB's earlier recommendations.

The goal of the Workgroup teleconference was to (1) seek clarification on some elements of the OPP summary document and (2) identify a set of criteria for assessing the sampling design that could be fairly and consistently applied to protocols from the AHETF and AEATF that will come before the Board at a later HSRB meeting.

<u>Points for Clarification</u>

The Workgroup wanted to learn how OPP intended to use the data from the AHETF and AEATF studies, and, thus, sought clarification for the Board on a number of issues related to the design and collection of the data.

Point #5 of the EPA Summary stated that "EPA has determined that generation of handler exposure data using a purposive diversity sampling (PDS) design is

acceptable" based on (a) the time and resources already expended on this design, (b) the delay and extra costs associated with developing a random sampling approach; and (c) the ability of these data to meet OPP's needs. "

OPP has informed the Task Forces that OPP expects their submissions to include scenario-specific justification of their proposed sampling strategies. For example, in the case of research on agricultural handlers' exposure, the justification should contain full documentation of:

a. The methods and rationale for selection of locale, study site, crop, equipment, workers, etc.,
b. Relevant agricultural statistics and production figures, chemical sales/use data, a description of the equipment to be used and a rationale for considering this equipment to be representative for the scenario.
c. Identification of all professional contacts who contributed information to the design process, with a description of their position, expertise, and experience;
d. Incorporation of random elements to be considered in each scenario-specific design, and an explanation as to how they will be implemented whenever feasible.
e. Cost estimates for all alternatives considered, documenting the basis and rationale for all estimates, including estimated costs of rejected alternatives.

To the extent that the materials provided by the Task Forces do not contain adequate information, OPP expects to ask clarifying questions to the TFs.

There was general agreement among Workgroup members and OPP that (a) the current PHED data set has many limitations and that it is advisable to obtain a better database on handler exposure for use in future risk assessments in almost all cases; and (b) a randomized sampling strategy would support some statistical analyses of data that are precluded by the use of a PDS design. The remainder of the discussion was aimed at ascertaining the extent to which data generated by PDS might produce useful data. Below are the clarification questions posed to William Jordan and a summary of his responses.

INFORMATION SESSION

Did the Task Forces provide detailed information on why randomized sampling would be excessively expensive?

No. OPP does not have a specific estimate of the likely increased cost of a randomized sampling design for any scenarios. The consultant to EPA confirmed that a randomized sampling design would be expected to be more expensive, probably significantly so, and primarily because of higher costs to identify candidates and recruit subjects. The consultant also acknowledged the difficulty in identifying potential participants in the studies and that ultimately, whether in a purposive or random sampling scheme, these

participants may be the same. For most scenarios too little is known about the target population even to estimate with confidence the cost of a randomized sample design.

Were there other reasons, in addition to those listed in the Summary that OPP decided to accept the PDS design?

In addition to considerations of the value of the data and the cost and feasibility of different sampling approaches, OPP also considered how a decision to insist on having the TFs use random sampling strategies would affect the timing of data generation. Assuming that the TFs agreed to use a probability based sampling strategy, OPP estimates that redesigning the AHETF and AEATF exposure monitoring programs to incorporate a randomized sampling design would probably delay data submission by another year or longer. The TFs, however, have informed OPP that the cost of employing random sampling strategies would significantly increase the testing costs, to a point that they would no longer be able to afford to conduct the research. They indicated they would consider ending the program or significantly reducing the number of monitoring units per scenario. If the TFs refused to develop the data voluntarily, OPP would have to issue Data Call-In notices to compel the pesticide industry to generate handler exposure data. Preparing and issuing DCIs would probably take OPP at least several years, with no assurance that a regulatory requirement for the data would be approved by the Government. Data generation and submission would take several more years. Given the acknowledged limitations of PHED, OPP thinks these likely delays and the uncertainty of the eventual outcome would not be in the best interests of currently exposed pesticide handlers.

How does OPP intend to use the AHETF and AEATF data?

OPP plans to (a) generate conservative exposure estimates based on the use of the high-end of the distribution and other information and (b) determine whether exposure is proportional to the amount of active ingredient handled in each scenario monitored. More specifically, OPP plans to use the data for each scenario in at least these ways:

1) To generate estimates of mid-range and high-end exposure from the distribution of the data.
2) To determine how the amount of active ingredient handled relates to exposure.
3) Determine if the proportionality assumption is not supported by data, to look for other variables that might have significant influences on exposure in order to develop hypotheses for examination and control in future studies.

Can an estimate of uncertainty for high-end values be determined with the PDS design?

No

Does the OPP's decision to accept PDS mean that sponsors are not expected to use randomized designs when possible?

No. Sponsors are expected to incorporate random elements into the design whenever that is feasible—as for example, when lists are available to identify the universe of relevant sites and when obtaining or generating such a list is practical and economically feasible.

Are there sampling requirements for PDS protocols?

Yes. Each scenario-specific design document must specify the sampling frame. OPP will evaluate the frame for representativeness and bias.

WORK GROUP DISCUSSION AND RECOMMENDATIONS TO THE FULL HSRB

The Work Group discussed the potential implications of the written materials and information session on protocol submissions, OPP presentations and HSRB review at the April Meeting. The Work Group concluded that it would recommend to the HSRB that:

1. Random sampling designs are preferred.
2. When random sampling is not possible, a PDS protocol must nonetheless have a well-developed sampling frame based on knowledge of the range of ingredient concentrations and distribution of methods used in the field.
3. Each protocol should be individually assessed for the feasibility of random assignment. When random sampling is not possible each protocol should be individually assessed for the adequacy of the PDS sampling frame.

With respect to the format of protocols submitted to OPP/HSRB, the protocols should include:

1. A detailed description of the methods and rationale for data collection (e.g., neck wipes)
2. If random sampling is not used, a detailed description of efforts made to incorporate random elements in each scenario-specific design and why it was not feasible (in terms of availability of information, costs, and time) to obtain a random sample.
3. For both random and PDS designs, a detailed description, rationale and justification for the scenario, selection of clusters, and what will be done within each cluster and why.
4. For all protocols, a detailed explanation of how data will be analyzed and interpreted by AHETF & AEATF.
5. For all protocols a detailed explanation of how the data is anticipated to be analyzed by EPA and how it will be useful for EPA risk assessments.

With respect to the format of OPP presentations to the Board:

1. OPP should develop a written glossary of terms (e.g., cluster, scenario) for HSRB and public reference. This glossary should be distributed but not summarized during OPP presentations.

2. For each protocol OPP should provide a brief (1 page if possible) abstract in terms appropriate for a lay audience describing the nature and purpose of the study and how EPA intends to use the data.
3. OPP's oral presentation should *not* focus on details. The Work Group believes that such detailed presentations distract from focusing attention on those aspects of the protocol for which OPP is eliciting Board feedback.
4. OPP's oral presentation on the science should not be a summary of the protocol, but a focused discussion of OPP's evaluation of why they think the study has sufficient scientific validity; the presentation should include questions regarding scientific validity that OPP wishes the Board to address.
5. OPP's oral presentation should also include a description of how the Agency plans to analyze and use the data.
6. Similarly, OPP's oral presentation should not focus on the details regarding the protection of the human subjects as such details are described in the written materials. Rather, a brief oral presentation should identify those aspects of the design that OPP believes raise human subjects concerns.

With respect to the participation of members of the AHETF and AEATF at HSRB meetings:

1. Since the HSRB makes its recommendations to EPA and not directly to sponsors, it is the responsibility of OPP and not the sponsor to present the protocol to HSRB, along with EPA's critique and conclusions.
2. Sponsors have the opportunity to express their perspectives and clarify information during public statement periods.
3. During Board discussion of protocols, sponsors should be available for additional clarifications that may be needed.
4. In addition, if sponsors believe that a specific point has not been adequately addressed they should have the opportunity to alert OPP to their concerns during the time allotted to the protocol; OPP in consultation with the Chair and DFO may recommend to the Board that the sponsor be heard on this issue.

With respect to criteria for "expedited review" of protocols in the future:

1. The Work Group agrees with OPP that an expedited review process is desirable for protocols similar to those that have already been evaluated by OPP and the Board.
2. The Work Group believes such a process can be developed only after the HSRB has had experience evaluating exemplary protocols.