AGENDA
U.S. ENVIRONMENTAL PROTECTION AGENCY (EPA)
FIFRA SCIENTIFIC ADVISORY PANEL (SAP)
OPEN MEETING
JULY 29-JULY 31, 2014
FIFRA SAP WEB SITE http://www.epa.gov/scipoly/sap/
DOCKET NUMBER: EPA–HQ–OPP–2014–0331
U.S. ENVIRONMENTAL PROTECTION AGENCY
CONFERENCE CENTER LOBBY LEVEL
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2777 S. CRYSTAL DRIVE, ARLINGTON, VA 22202

Scientific Issues Associated with New High Throughput Methods To Estimate Chemical Exposure

Please note that all times are approximate (see note at the end of the Agenda).

Day 1
Tuesday, July 29, 2014

9:00 A.M. Opening of Meeting and Administrative Procedures -- Fred Jenkins, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. Introduction and Identification of Panel Members -- James McManaman, Ph.D., FIFRA Scientific Advisory Panel Session Chair

9:10 A.M. Welcome and Opening Remarks – David Dix, Ph.D., Director, Office of Science Coordination and Policy (OSCP), EPA

9:20 A.M. Introduction and Overview: New High Throughput Methods to Estimate Chemical Exposure -- Alan Dixon, Exposure Assessment Coordination and Policy Division (EACPD, OSCP), EPA

Exposure Prioritization with ExpoCast Research

10:00 A.M. A Framework for High Throughput Exposure (HTE) Estimation -- John Wambaugh, Office of Research and Development (ORD), and National Center for Computational Toxicology (NCCT), EPA

10:30 A.M. Break

10:45 A.M. High Throughput Forward Prediction of Human Exposure -- Peter P. Egeghy, Ph.D. M.P.H., National Exposure Research Laboratory (NERL), ORD, EPA

11:05 A.M. Inference (Reverse Prediction) of Human Exposure -- Woodrow Setzer, National Center for Computational Toxicology (NCCT), ORD, EPA

11:35 A.M. Systematic Empirical Evaluation of Models (SEEM) Analysis and High Throughput Exposure Estimates -- John Wambaugh, ORD, NCCT, EPA

12:00 P.M. Lunch

High Throughput Toxicokinetics (HTTK) and Reverse Toxicokinetics (RTK)

1:00 P.M. High Throughput Toxicokinetics (HTTK) and Reverse Toxicokinetics (RTK) for the Endocrine Disruptor Screening Program (EDSP) -- John Wambaugh ORD, NCCT, EPA

Ongoing Research Needs: Ecological Exposure Predictions

2:10 P.M. High Throughput Ecological Exposure Modeling -- Craig Barber, Ph.D. NERL, ORD, EPA

2:35 P.M. Break

2:50 P.M. Evaluation Data and Statistical Framework for Ecological Exposure Predictions -- Woodrow Setzer, NCCT, ORD, EPA

Ongoing Research Needs: Near Field Human Exposure Modeling

3:10 P.M. Toward a Third Generation SEEM Analysis: New Data and Models -- Kristin Isaacs, Ph.D. NERL, ORD, EPA

Future Applications

3:50 P.M. EDSP Integrated Activity and Exposure Based Prioritization and Screening – Steven Knott, Director**,** EACPD, OSCP, EPA

4:35 P.M. Adjourn

Day 2
Wednesday, July 30, 2014

9:00 A.M. Opening of Meeting and Administrative Procedures – Fred Jenkins, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. Introduction and Identification of Panel Members – James McManaman, Ph.D., FIFRA Scientific Advisory Panel Session Chair

9:10 A.M. Follow-up from the Previous Day Presentations

10:00 A.M. Public Comments

10:45 A.M. Break

11:00 A.M. Public Comments (Cont'd)

12:00 P.M. Lunch

1:00 P.M. Charge to Panel

Charge Question 1.1. In the absence of sufficient exposure information to estimate exposure for the majority of the chemicals of interest in the Endocrine Disruption Screening Program (EDSP) using EPA's historical low-throughput methods, please comment on whether the Systematic Empirical Evaluation of Models approach (SEEM) is scientifically sound and suitable for using High Throughput Exposure (HTE) methods to estimate relative levels of chemical exposures and the associated uncertainty of these estimates for consideration in a prioritization approach.

2:00 P.M. Charge to Panel

Charge Question 1.2 Please suggest the most important steps for EPA that could decrease uncertainties and increase confidence in using the HTE approach to predict exposures in various demographic groups (e.g., young children, women of child bearing age) for large numbers of chemicals.

2:45 P.M. Break

3:00 P.M. Charge to Panel

Charge Question 2.1. In the absence of sufficient empirical toxicokinetics information for the thousands of EDSP relevant chemicals, please comment on the approach of using High Throughput TK (HTTK), High Throughput PBTK (HTPBTK), *In Vitro-In Vivo* Extrapolation (IVIVE), and Reverse Toxicokinetics (RTK) for estimating chemical TK to provide an

administered dose context to the concentrations showing bioactivity in the endocrine-related High-throughput screening (HTS) assays.

4:00 P.M. Charge to Panel

Charge Question 2.2. A comparison of the HTTK-predicted steady-state blood concentrations with *in vivo* values from the literature suggests that the overall correlation is low, but that the discrepancy between the two can be predicted using a combination of chemical properties, quantitative structure activity relationships (QSAR), and cutoffs from the HTTK assays. Please comment on: a) how well this approach characterizes the uncertainty in the steady-state blood concentrations, and b) whether the identification of chemical classes that need additional TK investigation is useful in a chemical prioritization or initial screening context.

5:00 P.M. Adjourn

Day 3
Thursday, July 31, 2014

9:00 A.M. Opening of Meeting and Administrative Procedures – Fred Jenkins, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

9:05 A.M. Introduction and Identification of Panel Members – James McManaman, Ph.D., FIFRA Scientific Advisory Panel Session Chair

9:10 A.M. Follow-up from the Previous Day Discussions

9:20 A.M. Charge to Panel (Cont'd)

Charge Question 2.3. Please comment on whether the assumptions made in these models are appropriate given the current state of the science and data limitations.

10:00 A.M. Charge to Panel

Charge Question 2.4. Please suggest the most important steps EPA should take to improve the various kinetic models to provide rapid and cost-effective predictions for large number of chemicals.

10:45 A.M. Break

11:00 A.M. Charge to Panel

Charge Question 2.5. Please comment on the approaches presented in the present White Paper for comparing RTK-derived endocrine-active dose ranges with exposure predictions from ExpoCast. Discuss the strengths and limitations of these comparisons, and whether this or other approaches are suitable for clearly distinguishing chemicals with higher predicted doses from chemicals with lower predicted RTK adjusted doses.

12:00 P.M. Lunch

1:00 P.M. Charge to Panel (Cont'd)

Charge Question 3.1. Please comment on the three key areas including whether there are other areas that are of equal or higher priority to support an integrated activity/hazard and exposure based prioritization and screening approach within the EDSP or other chemical programs.

1:45 P.M. Charge to Panel

Charge Question 3.2. We propose applying the ExpoCast framework to ecological exposures using aggregated water monitoring data to evaluate the predictions of environmental fate and transport models. Please identify other data, models or environmental media that may be of greater value in the initial model calibration and uncertainty analysis.

2:30 P.M. Break

2:45 P.M. Charge to Panel

Charge Question 3.3. Please identify other relatively high-throughput sources of exposure-related information that should be included in these three key areas and suggest how this information would be used to help prioritize chemicals.

3:45 P.M. Charge to Panel

Charge Question 3.4. For the HTTK work going forward, please comment on additional studies that could be performed or approaches that could be taken to improve rapid and cost efficient predictions of TK for large numbers of chemicals.

4:30 P.M. Closing Remarks – James McManaman, Ph.D., FIFRA Scientific Advisory Panel Session Chair
Fred Jenkins, Ph.D., Designated Federal Official, Office of Science Coordination and Policy, EPA

5:00 P.M. Adjourn

Note: Please be advised that agenda times are approximate; when the discussion for one topic is completed, discussions for the next topic will begin. For further information, please contact the Designated Federal Official for this meeting, Dr. Fred Jenkins, via telephone: (202) 564-3327; fax: (202) 564-8382; or email: jenkins.fred@epa.gov.