



Children's Health Symposium
February 25 and 26, 2014
Cal/EPA building, 1001 I St., Sacramento, CA
Sierra Hearing Room



Symposium 2014 Theme: Impacts of Environmental Chemicals on Development – Are complex interactions captured by traditional risk assessment practices?

The multi-disciplinary study of the effects of environmental stressors on infants and children is increasing our understanding of the complex relationships between exposure to environmental chemicals and effects on development, child and lifelong health. While typical animal toxicity studies can help define the toxicological characteristics of chemicals and provide information on which to base a regulatory risk assessment, they cannot tell us about impacts of other factors, including multiple chemical exposures and non-chemical stressors, on human response to environmental chemicals. Current human and animal research on response to chemicals, associations between environmental exposures and disease, and the literature on interactions between non-chemical stressors and toxicants paint a complex picture. Further, the push towards integrating information from in vitro assay systems, including the newer high throughput test systems results (e.g., Tox 21), computational toxicology, and read-across methods will be providing us with “non-traditional” toxicity data. How will we utilize these types of information in assessing hazards and risks from environmental chemical exposures?

Our current methods of risk assessment try to capture the complexity in general ways. For example, we use dose-response information for the most sensitive endpoint and most sensitive species, and uncertainty factors to account for interspecies extrapolation and inter-individual variability in response to a toxicant in the human population in non-cancer assessment. We weight carcinogen exposures that occur early in life when assessing cancer risk. Much uncertainty remains, and the newest scientific findings are forcing a re-thinking of risk assessment generally.

Continuing to educate ourselves is necessary to begin to address how we can more effectively conduct risk assessment. We are providing a forum in this symposium to hear some of the latest science regarding impacts of chemical exposures during development. This is a broad topic and thus we are focusing in three areas: 1) epigenetic changes from environmental exposures; 2) impacts of toxicants on the developing lung and brain; 3) new in vitro methods for assessing potential for developmental toxicity.

The goals of this symposium are to get regulatory scientists in California thinking about:

- How to incorporate complex interactions into risk assessment, particularly for early life exposures;
- How to incorporate information from new toxicity testing paradigms into risk assessments now; and

- How to incorporate impacts of non-chemical stressors that increase vulnerability, and whether current methods of risk assessment adequately account for at least some of the vulnerabilities (e.g., use of weighting factors in cancer risk assessment, use of uncertainty factors).

Sponsors: California Environmental Protection Agency, Office of Environmental Health Hazard Assessment (OEHHA). Children's Environmental Health Program; UCSF Pediatric Environmental Health Specialty Unit.



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Agenda

DAY 1 **TUESDAY, FEBRUARY 25, 2014**

8:45 – 9:00 Welcome and Overview – George Alexeeff, Executive Director, OEHHA;
Melanie Marty, Assistant Deputy Director, Division of Scientific Affairs

SESSION 1. Developmental Exposure to Toxicants - Influence of Chemicals and Non-chemical Stressors on the Epigenome and Subsequent Health Outcomes

9:00 – 9:45 Epigenetic Impact of Prenatal Exposure to Adversity
Presenter: Frances Champagne, Columbia University

9:45 – 10:30 What is a Mixture? Defining the Complexity of Environment for
Research on Child Development
Presenter: Bob Wright, Mt. Sinai School of Medicine, New York City

10:30 – 10:50 Break

10:50 – 11:35 Epigenetics at the Interface of Genetic and Environmental Risk Factors
in Autism-Spectrum Disorders
Presenter: Janine LaSalle, University of California, Davis

11:35 – 12:05 Panel discussion
Panelists: Frances Champagne
Bob Wright
Janine LaSalle
Moderator: Mark Miller

12:05 – 1:30 Lunch

SESSION 2. Environmental exposure and developmental outcome

1:30 – 2:15 Maternal Stress and Pollution: Rewiring Brain in Offspring
Presenter: Richard Auten, Duke University

2:15 - 2:55 Early Life Exposure to Arsenic, Cancer and Respiratory Health
Outcomes in a Human Population
Presenter: Craig Steinmaus, Cal/EPA, OEHHA

2:55 – 3:15 Break

- 3:15 – 4:00 Bisphenol A Alters Cellular Development of the Conducting Airway
 Presenter: Laura Van Winkle, University of California, Davis
- 4:00 – 4:30 Panel discussion
 Panelists: Richard Auten
 Craig Steinmaus
 Laura Van Winkle
 Moderator: Lauren Zeise
- 4:30 Adjourn Day 1

DAY 2 WEDNESDAY, FEBRUARY 26, 2014

Session 3. Tox21 Developmental toxicity models

- 8:45 – 9:00 Introduction to Day 2 and Overview of Sessions – Melanie Marty
- 9:00 – 9:40 *In Vitro* Assays and *In Silico* Models for Assessing Developmental
 Toxicity: Progress and Challenges
 Presenter: Tom Knudsen, USEPA.
- 9:40 – 10:20 Use of In Vitro Developmental Neurotoxicity Assays - Evaluating
 Anesthetics.
 Presenter: Merle Paule, NCTR, FDA
- 10:20 – 10:40 Break
- 10:40 – 11:10 Respondent: Translating and Integrating Tox 21 DNT for Risk
 Assessment: Challenges and Opportunities-Where are we?
 Presenter: Elaine Faustman, University of Washington
- 11:10 – 12:00 Open Discussion with All Participants (Speakers and Audience)
 Panelists: Tom Knudsen
 Merle Paule
 Elaine Faustman
 Bob Wright
 Janine LaSalle
 Richard Auten
 Craig Steinmaus
 Laura Van Winkle
 Lauren Zeise
- Moderator: Melanie Marty
- 12:00 – 12:15 Concluding remarks

12:15

Adjourn Symposium

Open Discussion – Audience and All Speakers

- How can we use information on complex interactions in risk assessment? Can we use these types of data only qualitatively?
- How can we account for multiple chemical exposures in risk assessment, other than the Hazard Index approach for non-cancer effects and the assumption of additivity for cancer effects?
- Are we adequately including impacts of non-chemical stressors in our typical risk assessment paradigm for non-cancer health impacts?
- Can we use the data arising from Tox21 assays in risk assessment? Is there a path forward to use Tox21 types of assays and data resulting therefrom in hazard identification? Dose-response assessment?