

THE NATIONAL ACADEMIES

Advisers to the Nation on Science, Engineering, and Medicine

Board on Environmental Studies and Toxicology

NATIONAL RESEARCH COUNCIL
SIXTH WORKSHOP OF THE STANDING COMMITTEE ON
RISK ANALYSIS ISSUES AND REVIEWS

CHARACTERIZING THE POTENTIAL HUMAN TOXICITY FROM
LOW DOSES OF PHARMACEUTICALS IN DRINKING WATER:
ARE NEW RISK ASSESSMENT METHODS OR APPROACHES REQUIRED?

Public Meeting: December 11-12, 2008

National Academy of Sciences

2101 Constitution Avenue, NW

Lecture Room

Washington, DC 20418

PUBLIC AGENDA – December 11, 2008

- 9:00 Introduction and Purpose of the Workshop Bernard Goldstein, Committee Chair
- 9:05 Overview of EPA's Goals for the Workshop Peter Preuss, Director
National Center for Environmental Assessment, EPA
Suzanne Rudzinski, Deputy Director
Office of Science and Technology, EPA
- 9:15 Overview of Workshop Format and Issues to be Discussed Joyce Tsuji
Committee

THE FDA REVIEW PROCESS FOR PHARMACEUTICALS

- 9:20 Considerations Regarding Drug Approval Process at FDA Raanan Bloom
Center for Drug Evaluation and Research, FDA
Charles Eirkson, III
Center for Veterinary Medicine, FDA

EXPOSURE TO PHARMACEUTICALS IN DRINKING WATER

- 10:00 What's in Our Water? Rolf Halden
Arizona State University
- 10:40 ***BREAK***

ARE PHARMACEUTICALS DIFFERENT FROM OTHER ENVIRONMENTAL CONTAMINANTS

10:50 What Makes Pharmaceuticals Potentially Different? David Cragin
Merck

WHAT DATA ARE POTENTIALLY AVAILABLE ON PHARMACEUTICALS

11:30 Are Pharmaceuticals Data-Rich Compounds? Roger Meyerhoff
Lilly Research Laboratories

12:00 The Value of Human Clinical Studies for Risk Assessment Philip Guzelian
University of Colorado

12:30 LUNCH BREAK

1:30 **PANEL DISCUSSION** – [*Speakers, Committee Members, and Invited Panelists (Edmund Crouch, Cambridge Environmental, Inc.; Ronald Hines, Medical College of Wisconsin; Edward Sargent, University of Medicine and Dentistry of New Jersey and EV Sargent LLC; Rick Schnellmann, Medical University of South Carolina; Lauren Zeise, California EPA). Questions to be addressed include the following: Are drug safety databases adequate for chronic, low-dose exposure assessments? Are data available that allow us to use chemical-specific data rather than general defaults that we typically rely on for other environmental contaminants?]*

RISK ASSESSMENT OF PHARMACEUTICALS

2:15 Risk Assessment Practices at EPA Peter Preuss, Director
National Center for Environmental Assessment

2:35 Issues in Identifying Margins of Exposure for Pharmaceuticals in Drinking Water and in Evaluating their Adequacy Joe Rodricks
ENVIRON

3:15 Possible Roles of Pharmacokinetic and Pharmacodynamic Data in Evaluating Margins of Exposure Harvey Clewell
The Hamner Institutes for Health Sciences

3:55 BREAK

4:15 **PANEL DISCUSSION** – [*Speakers, Committee Members, and Invited Panelists (Edmund Crouch, Cambridge Environmental, Inc.; Ronald Hines, Medical College of Wisconsin; Edward Sargent, University of Medicine and Dentistry of New Jersey and EV Sargent LLC; Rick Schnellmann, Medical University of South Carolina; Lauren Zeise, California EPA). Questions to be addressed include the following: What point of departure is most appropriate for quantifying potential hazard from exposure to low doses of pharmaceuticals? How can the likely more extensive pharmacologic information on pharmaceuticals be used to evaluate potential effects at low doses? Does the application of uncertainty factors, particularly for potentially sensitive populations, differ for pharmaceuticals? What factors would make the application different? Can the pharmacologic data be used to develop pharmacokinetic models to evaluate the impact of metabolic enzyme polymorphisms and other interindividual differences at low doses? How best do we characterize the potential for adverse effects in the general population—including groups sensitive because of age, gender, genetics, or other factors—from chronic low doses of pharmaceuticals and their breakdown or metabolic products?]*

5:15 Public Comment

5:30 **ADJOURN PUBLIC SESSION**

PUBLIC SESSION – DECEMBER 12, 2008

INTERNATIONAL PERSPECTIVE

9:00 European Perspective on Risk Assessment of Pharmaceuticals Hans Sanderson
National Environmental Research Institute of Denmark

SINGLE CHEMICAL VS CUMULATIVE RISK ASSESSMENT

9:30 Considerations for Single Chemical vs Mixture Risk Assessment Christopher Borgert
Applied Pharmacology and Toxicology, Inc.,
University of Florida

DATA GAPS AND CHALLENGES

10:00 EPA's Perspective on Data Gaps and Challenges Hal Zenick
Director, National Health and
Environmental Effects Research Laboratory

10:30 **PANEL DISCUSSION** – *[Speakers, Committee Members, and Invited Panelists (Edmund Crouch, Cambridge Environmental, Inc.; Ronald Hines, Medical College of Wisconsin; Edward Sargent, University of Medicine and Dentistry of New Jersey and EV Sargent LLC; Rick Schnellmann, Medical University of South Carolina; Lauren Zeise, California EPA). Questions to summarize discussion at workshop and to focus on overall approach to pharmaceuticals and distinguish how pharmaceuticals are different from other environmental chemicals and whether standard risk assessment practices would need to be modified. Such questions would include the following: Does the pharmacologic activity of a pharmaceutical inherently change assumptions about how to assess human risk from low-dose exposures? As one moves from a single-chemical risk assessment to a multi-chemical risk assessment, what are the key questions to ask to focus the assessment? What are the potential approaches for evaluating the combined effect of pharmaceuticals?]*

11:30 Public Comment

12:00 **ADJOURN WORKSHOP**