

Beyond Science and Decisions: From Problem Formulation to Dose-Response. Workshop IV

Date: May 22-24, 2012

Location: TCEQ, Austin, TX

Introduction

- ▶ Dose–Response Advisory Committee (DRAC)
- ▶ Alliance for Risk Assessment (*ARA*) Steering Committee
- ▶ Sponsors

Dose-Response Advisory Committee

- ▶ Rick Becker, American Chemistry Council (ACC)
- ▶ Tiffany Bredfeldt, Texas Commission on Environmental Quality (TCEQ)
- ▶ Michael Dourson, Toxicology Excellence for Risk Assessment (TERA)
- ▶ Julie Fitzpatrick, Environmental Protection Agency (EPA)
- ▶ Roberta Grant, TCEQ
- ▶ Lynne Haber, TERA
- ▶ Lynn H. Pottenger, The Dow Chemical Company
- ▶ Jennifer Seed, EPA

ARA Steering Committee

- ▶ Anita Meyer, United States Army Corps of Engineers
- ▶ Annette Dietz, Oregon Department of Environmental Quality
- ▶ Bette Meek, University of Ottawa/Health Canada
- ▶ Edward Ohanian, United States Federal Employee
- ▶ Michael Honeycutt, Texas Commission on Environmental Quality
- ▶ Ralph Perona, Neptune & Company, Inc.
- ▶ Ruthann Rudel, Silent Spring
- ▶ William Hayes, State of Indiana
- ▶ Michael Dourson, Toxicology Excellence for Risk Assessment (TERA) (recused)



Thanks to our sponsors!



48 sponsors and collaborators:



• 12 government agencies



• 12 industry groups



• 7 scientific societies



• 9 non-profit

organizations/consortia



• 8 consulting groups



INDUSTRIAL ECONOMICS, INCORPORATED

Purpose

- ▶ To advance the recommendations of NAS (2009) and subsequent framework of *ARA* (2012) on problem formulation and dose–response analysis, through review of illustrative case studies for further development of methods.

Fourth in the Series of Workshops

- ▶ **Workshop I**
 - TCEQ, March 16–18, 2010
- ▶ **Workshop II**
 - Crystal City, Virginia (in tandem with the Federal & State Risk Assessment & Toxicology Committee), October 11–13, 2010
- ▶ **Workshop III**
 - Noblis; Falls Church, Virginia, May 4–6, 2011
- ▶ **Workshop IV**
 - TCEQ, May 22–24, 2011

Overview of Workshop Objectives

- ▶ Build off the NAS (2009) report
 - Develop practical guidance for use by risk managers at a variety of levels
 - States, regional managers, various agencies, & industry
 - Risk assessment techniques applicable to specific problem formulations.
- ▶ Implement a multi-stakeholder approach to share information, ideas, and techniques in support of developing practical, problem-driven risk assessment guidance.

Housekeeping

- ▶ Look around now for exits in case of fire
- ▶ Cell phone reminder....
- ▶ Mid-morning and afternoon breaks
- ▶ Lunch speakers scheduled and lunches provided on Wednesday and Thursday
- ▶ The sessions are being webcast so remember there is a second audience listening on the phone. Please be mindful of their participation:
 - Use the mics to facilitate listening for those on webcast
 - Only one person speaking at a time
 - Identify yourself with name & affiliation when speaking

Workshops I–III Summary

- ▶ ~100 participants for each (webcast + in-person)
- ▶ 28 Case studies evaluated by Science Panel
- ▶ Framework for linking problem formulation & methodologies was developed & refined

Updates from DRAC

- ▶ **SRA 2011: Double Symposium (Chairs: Fitzpatrick & Becker): Pressing Forward: Improving problem formulation & dose-response beyond “Science & Decisions”**
- ▶ **SOT 2012: 6 presentations**
 - 2 case study presentations in “top 10” abstracts from RASS;
 - Current case study in “top 10” papers for 2011 from RASS
- ▶ **Manuscript: A Framework for “Fit for Purpose” Dose-Response Modeling for Risk Assessment (Meek *et al.*)**
- ▶ **World Congress SRA 2012 (Australia!) Symposium (Chairs: J. Fitzpatrick & M. Hartley): Advances in Risk Assessment Methodologies**
- ▶ **SRA 2012 Symposium proposed (Chairs: Fitzpatrick & Pottenger): Putting It All Together: Recent Developments in Risk Assessment Approaches**

Workshop IV

- ▶ Workshop IV marks the transition to an evergreen approach, envisioned to be a continuing semi-annual workshop series to explore and review recent advances in risk assessment and dose-response assessment.



Workshop IV & beyond: Evergreen & Standing Science Panel

- ▶ Evergreen
 - Two meetings/year: 1 in-person, 1 web-based
 - Transition to self-supporting, sustainable effort:
 - case studies brought to Science Panel for review/discussion
- ▶ Standing Science Panel Role:
 - Provide input on case study methods being proposed to enhance the risk framework.
 - Provide input on the utility of the case study methods to address specific problem formulations,
 - Identify areas for additional development of the case study and/or method.
 - Inclusion of a method or case study in the framework as an illustration of a technique does not imply panel acceptance of the chemical-specific outcome.

Workshop IV & beyond: Standing Science Panel Selection

- ▶ Standing Science Panel Process:
 - Advertised for nominations (self or otherwise)
 - Previous panel asked about continued service
 - Received 25 nominations
 - *ARA* steering committee selected Standing Science Panel members
- ▶ Aim to include diverse range of expertise & affiliations
 - 9 standing Science Panel members
 - 1 alternate
 - 8 *ad hoc* – address particular subject areas

Workshop IV & beyond: Standing Science Panel Affiliations

- ▶ Diverse Range of Affiliations:
 - 2 from the US Federal Government (EPA)
 - 2 from industry
 - 1 from academia
 - 2 from state government
 - 1 from nonprofit group
 - 1 consultant
 - 1 member of the NAS *Science & Decisions* Panel
 - Plus 1 *ad hoc* member Workshop IV: consultant

Standing Science Panel Members

- ▶ *Richard Beauchamp, Texas Dept State Health Services*
- ▶ *James S. Bus, The Dow Chemical Company*
- ▶ *Rory Conolly, U.S EPA NHEERL*
- ▶ *Mike Dourson, TERA*
- ▶ *R. Jeffrey Lewis, ExxonMobil Biomedical Sciences, Inc.*
- ▶ *Bette Meek, McLaughlin Centre for Population Health Risk Assessment, University of Ottawa (Chairperson)*
- ▶ *Greg Paoli, Risk Sciences International (NAS 2009 Panel)*
- ▶ *Rita Schoeny, U.S. EPA*
- ▶ *Alan Stern, New Jersey Dept of Environmental Protection*

- ▶ *Ad hoc Workshop IV member: Lorenz Rhomberg, Gradient*

Workshop Agenda: Day 1 (1:00 pm–5:30 pm)

- ▶ Welcome and Introduction & Updates:
 - Toby Baker, TCEQ, & DRAC members
- ▶ Keynote Address:

Incorporating New Technologies into Toxicity Testing and Risk Assessment: 21st C Vision to a Data-Driven Framework
Rusty Thomas, The Hamner Institutes for Health Sciences

- ▶ Presentation of *ARA* Framework: Lynne Haber, TERA
- ▶ EPA's Response to NAS Framework: Rita Schoeny, EPA
- ▶ Observer Comments

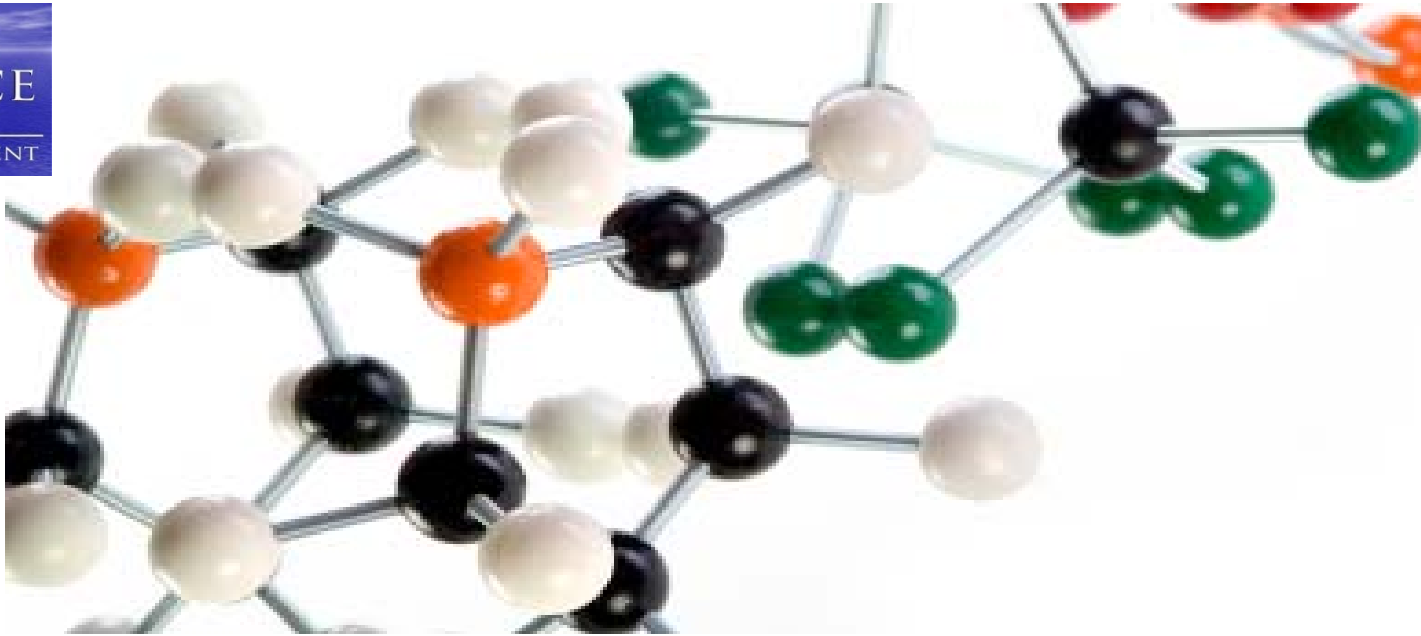
- ▶ Reception (heavy *hors d'oeuvres*, 6:30 to 9:00)

Workshop Agenda: Day 2 (8 am –5:30 pm May 23)

- ▶ **Case Study** (8 – 11:30 am):
 - Criteria Requirements for Data–Driven Carcinogenicity MOA Determinations: CHCl₃: Chris Borgert, Applied Pharmacology Toxicology Inc.
- ▶ **Lunch** (11:30 am –12:30 pm)
- ▶ **Updates** (12:30–2 pm)
 - EO Mode of Action (MOA) W. Gulledge, ACC
 - The Occupational Alliance for Risk Science (OARS) J. Perkins, UT Health Science Center
 - Naphthalene Mode of Action (MOA) L. Rhomberg, Gradient
 - Structure–Activity Relationships (SAR) Applied to Short Term Exposures: T. Bredfeldt, TCEQ
- ▶ **Case Studies** (2:30–5 pm):
 - Case Study Proposal: Value of Information: Eric Ruder, IEC
 - A Tiered Framework for Interpreting Human Biomonitoring Results: Rick Becker, ACC
- ▶ **Observer Comments** (5:00 to 5:30)

Workshop Agenda: Day 3 (8:30–noon, May 24)

- ▶ **Combined Exposures Framework and Discussion:**
Bette Meek, U. Ottawa
- ▶ **Case Studies (9:30 to noon):**
 - The Human Relevant Potency Threshold: Reducing Uncertainty by Human Calibration of Cumulative Risk Assessments: Chris Borgert, Applied Pharmacology Toxicology Inc.
 - Methods for Deriving Inhalation Effect Levels for Comparison to Health-Protective Values: Roberta Grant, TCEQ
- ▶ **Observer Comments and Closing remarks**



Beyond Science and Decisions: From Problem Formulation to Dose-Response. Workshop IV

Date: May 22-24, 2012

Location: TCEQ, Austin, TX



Workshop II/III Expert Panel

- ▶ 3 from the US Federal Government, with 2 from EPA
- ▶ 2 from industry
- ▶ 2 from academia
- ▶ 1 from state government, and 1 state government emeritus
- ▶ 2 from nonprofit groups
- ▶ 1 consultant
- ▶ 2 are members of the NAS *Science & Decisions* Panel

Activities between Workshops II & III

- ▶ Panel reviewed the case studies
- ▶ A draft risk framework was developed and posted on the ARA website
- ▶ New case studies were proposed and submitted to the Panel for consideration
- ▶ Panel used framework to identify areas and methodological issues where additional illustrative case studies were needed
- ▶ Those case studies were invited to be brought to Workshop III

Organizational Framework: Dose-Response Methods Presented

PHASE 1: Problem Formulation & Scoping

(Adapted from [NAS \[2009\] Figure S-1](#))

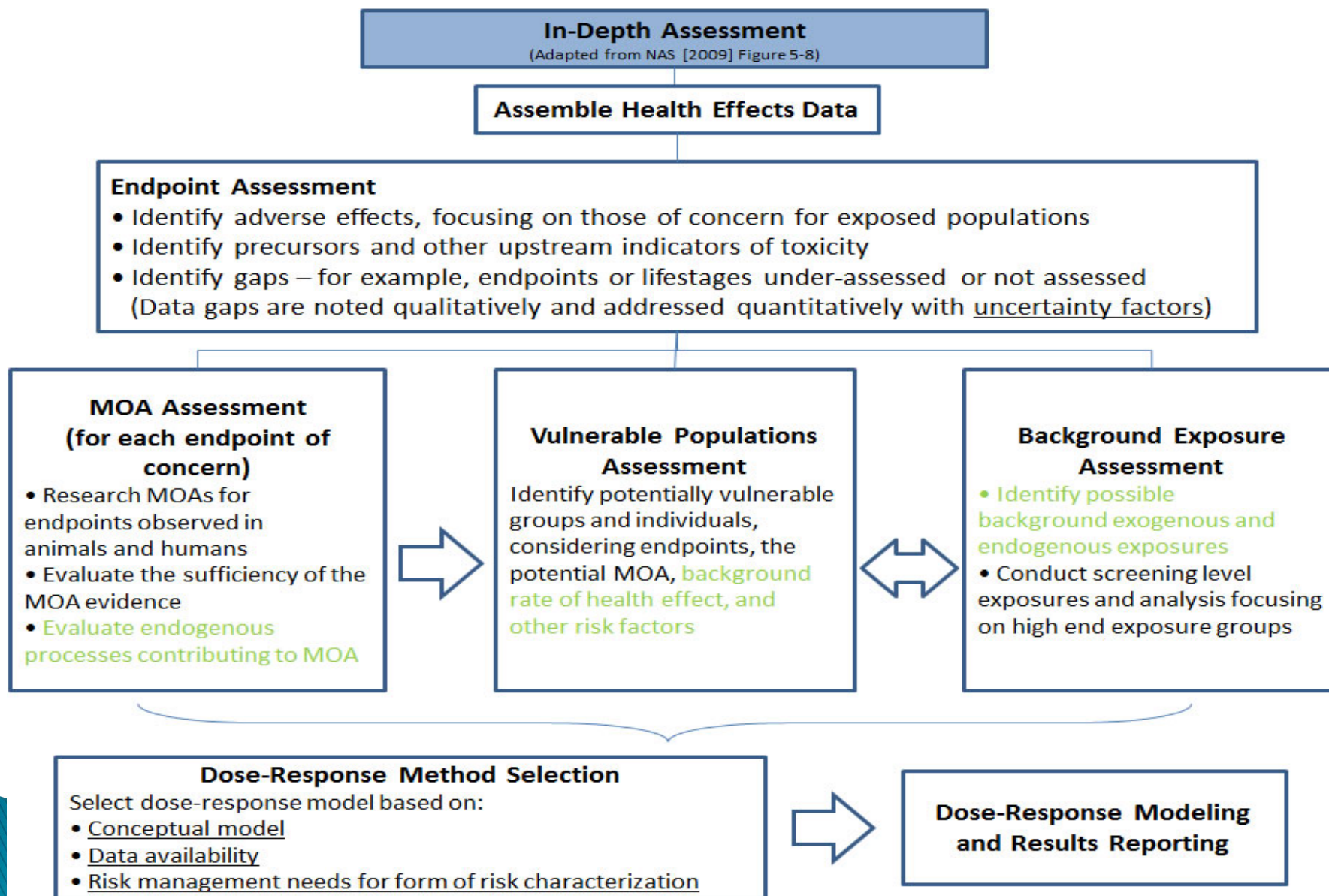
- What problem(s) are associated with existing environmental conditions?
- If existing conditions appear to pose a threat to human or environmental health, what options exist for altering those conditions?
- Under the given decision context, what risk and other technical assessments are necessary to evaluate the possible risk management options?

Qualitative Decision

Quantitative Screening
Decision

In-Depth Assessment

In-Depth Dose-Response Assessment



Workshop II/III Science Panel

- ▶ Provide guidance during the workshops
- ▶ Evaluate the case studies
- ▶ Use case studies to evolve methodologies and address cross-cutting issues raised in NAS *Science & Decisions* report
- ▶ Balance across affiliation & expertise
 - Risk assessment and Toxicology

ACC Center for Advancing Risk Assessment Science & Policy (ARASP) Perspective

- ▶ Group of chemical-specific groups working towards improving risk assessment science and policy, given changing world of toxicology.
- ▶ Accelerate the development, evaluation and use of weight-of-evidence frameworks, MOA analysis, & quantitative uncertainty methods in chemical risk assessments.
- ▶ Support ARA-sponsored workshops to broaden & deepen scientific discussion on dose-response assessment & MOA
 - Contribute case studies / scientific data & analyses and actively participate in the scientific discourse of the ARA project.

TCEQ's Perspective

- ▶ Commissioner's and executive management of the Texas Commission on Environmental Quality support these series of workshops
- ▶ Environmental regulations should be meaningful and provide the most benefit to those who need help
- ▶ Good science should lead the way and improve the process

EPA Perspective

- ▶ The case studies being developed by this workshop series will be useful to the Agency as it moves forward in addressing the recommendations presented in *Science and Decisions*.



Panel Selection Process

- ▶ Announcement of workshops, with a call for Panel nominations
- ▶ DRAC also nominated panel member candidates
- ▶ ARA Steering Committee reviewed candidates and developed a prioritized list of nominees
- ▶ Invitations were sent to a total of 27 people
- ▶ Particular effort was made to include people from the NAS, 2009 Panel & environmental NGOs