

**U.S. Environmental Protection Agency  
Science Advisory Board  
Dioxin Review Panel**

Public Teleconference  
June 24, 2010  
1:00 – 3:30 p.m. (Eastern Daylight Time)

**Attendance:**

*Members of the EPA Science Advisory Board (SAB) Dioxin Review Panel:*

Timothy Buckley (Chair), Harvey Clewell, Louis Anthony (Tony) Cox, Elaine Faustman, Scott Ferson, Jeffrey Fisher, Helen Hakansson, Russ Hauser, B. Paige Lawrence, Michael Luster, Paolo Mocarrelli, Victoria Persky, Sandra Petersen, Karl Rozman, Arnold Schechter, Allen Silverstone, Mitchell Small, Anne Sweeney, and Mary Walker. (See Attached Roster).

*SAB Staff:*

Thomas Armitage, Designated Federal Officer

*EPA Representatives:*

Annette Gatchett, EPA Office of Research and Development (ORD); Belinda Hawkins, EPA ORD; Glenn Rice, EPA ORD; Ravi Subramaniam, EPA ORD; Maria Spassova, EPA ORD; Jeff Swartout, EPA ORD; Linda Teuschler, EPA ORD; Linda Tuxen, EPA ORD; Janet Hess-Wilson, EPA ORD; Hisham El-Masri, EPA ORD

*Public (individuals who requested access to the teleconference):*

Todd Abel, Chlorine Chemistry Division, American Chemistry Council; John Buddy Andraide; William Blackley, Citizens Alliance for a Clean Healthy Economy; Ryan Black, Coastal Conservation League; Lesa Aylward, Summit Toxicology; Ann Bradley, Integral Consulting; Jimmy Bruce, Serious Chester County Residents Against Pollution; Pat Cassano, General Electric Company; Rita Chapman, Sierra Club Michigan Chapter; Joshua Cohen, Tufts University Medical Center; Roger Cooke, Resources for the Future; Sandrine Deglin, Exponent; Bridget DiCosmo, Risk Policy Report; Tracey Easthope, Environmental Health Project; John Festa; David B. Fischer, American Chemistry Council; Michael Greene, Center for Environmental Health; Gary Guggolz, U.S. Government Accountability Office; Donald L. Hassig, Cancer Action Network; Carl Herbrandson, Minnesota Department of Health; Cheryl Hogue, Chemical and Engineering News; Rick Hind, Greenpeace; Katie Huffling, Alliance of Nurses for Healthy Environments; Steven Huntley, Arcadis, Inc.; Russell E. Keenan, Integral Consulting; Steve Kopperud, Policy Directions, Inc.; Richard Krock, The Vinyl Institute;

Katherine Kurtz, Navy and Marine Corps Public Health Center; Judy Levin, Center for Environmental Health; Azita Mahayekhi, International Brotherhood of Teamsters; Joyce Martin, American Association on Intellectual and Developmental Disabilities; Teresa Mills; Olga Naidenko, Environmental Working Group; Michelle Hurd Riddick, Lone Tree Council; Pat Rizzuto, BNA, Inc.; Mike Schade, Center for Health, Environment, and Justice; John Schell, ENTRIX; Jay Silkworth, General Electric Company; Laura Solem, Minnesota Pollution Control Agency; Robert Spiegel, Edison Wetlands Association; Daniele Wikoff Staskal, ToxStrategies; Maureen Swanson, Learning Disability Association of America; Belvin Sweatt; Janice Valverde, Daily Environment Report BNA; Sarah Westervelt, Basel Action Network; Jane Williams, California Communities Against Toxics; Monica Wilson, Global Alliance for Incinerator Alternatives; Timothy C. Wolfson, Babst Calland Clements and Zomnir, PC.

**Purpose:**

The purpose of the teleconference was to provide information to the SAB Dioxin Review Panel to prepare for a meeting to review the draft document, *EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*. On the teleconference the Panel heard an overview presentation from EPA, received oral public comments, and discussed the charge questions and agenda for the upcoming review meeting.

**Summary of the Discussion:**

The meeting was announced in the Federal Register<sup>1</sup> and proceeded according to the meeting agenda<sup>2</sup>. Thomas Armitage, Designated Federal Officer (DFO) for the Dioxin Review Panel convened the teleconference at 1:00 p.m. Eastern Daylight Time and called the roll. He stated that the EPA Science Advisory Board (SAB) was a chartered federal advisory committee. He reviewed Federal Advisory Committee Act (FACA) requirements. He noted the Panel's compliance with ethics requirements. He stated that one Panel member, Dr. Paolo Mocarelli, had indicated that he would not participate in the discussion of the charge questions specifically pertaining to use of the Mocarelli et al. (2008) study (cited in the document, *EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*) in deriving the reference dose for dioxin. Dr. Armitage stated that, as DFO, he would be present during Panel business and deliberations. He stated that summary minutes of the teleconference would be prepared and certified by the Chair.

Dr. Timothy Buckley, Chair of the Dioxin Review Panel, reviewed the teleconference objectives and agenda. He stated that the purpose of the call was to provide the Panel with an overview of EPA's draft document, *Reanalysis of Key Issues related to Dioxin Toxicity and Response to NAS Comments* and to discuss the charge questions<sup>3</sup> and agenda for the upcoming Panel meeting. He stated that following an overview presentation by EPA, the Panel would hear public comments, ask EPA clarifying questions concerning the presentation, and discuss the charge questions and agenda for the July 13-15 face-to-face meeting.

Dr. Buckley stated that a second face-to-face meeting of the Panel would be held following the scheduled July 13-15 meeting. He stated that the second meeting was being held to provide the Panel with additional time to review EPA's document and receive public comments. He stated that at the first meeting, the Panel would discuss key issues to be addressed in the charge question responses but would not reach consensus.

*Overview of EPA's Draft Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*

Dr. Glenn Rice of EPA's Office of Research and Development provided an overview presentation<sup>4</sup> on the EPA Document, *Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*<sup>5</sup>. Dr. Rice reviewed the history of EPA's dioxin assessment and stated that EPA had developed the document being reviewed by the SAB Panel in response to recommendations from the National Academies of Sciences (NAS). He summarized the key recommendations of the NAS pertaining to the dose-response assessment of dioxin. He noted that the NAS had recommended: 1) improved transparency and clarity in the selection of key data sets for dose-response analysis; 2) further justification of approaches to dose-response modeling for cancer and noncancer endpoints; and 3) improved transparency, thoroughness, and clarity in quantitative uncertainty analysis. He further noted that NAS had encouraged EPA to calculate an oral reference dose.

Dr. Rice summarized key points in sections of EPA's draft document. He noted that the document delineated a selection process to identify 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) epidemiology and rodent bioassay studies that could serve as a principal studies for derivation of a reference value. Dr. Rice reviewed the criteria used to select the studies.

Dr. Rice noted that EPA's document applied physiologically-based pharmacokinetic (PBPK) modeling to calculate human equivalent doses of TCDD. He described important factors influencing TCDD pharmacokinetics and briefly described how EPA had used the Emond PBPK model to estimate lifetime average daily oral doses needed to achieve blood TCDD concentrations that occurred during animal bioassays, and to estimate the lifetime average daily doses that would correspond to the TCDD blood concentrations reported in epidemiology studies. He further noted that EPA's document provided a reference dose for noncancer effects and an oral slope factor for carcinogenicity for TCDD oral exposures, and addressed the feasibility of quantitative uncertainty analysis for TCDD dose-response assessment.

Dr. Rice discussed the derivation of the reference dose for dioxin. He described two human studies that had been designated as co-principal studies for deriving the RfD, and he briefly summarized how the RfD had been derived.

Dr. Rice discussed how EPA had derived the cancer oral slope factor for dioxin and indicated that EPA had identified limitations that precluded making strong conclusions based on nonlinear dose-response modeling exercises.

Dr. Rice discussed how EPA had addressed quantitative uncertainty analysis. He noted that EPA had determined that a comprehensive data driven quantitative uncertainty analysis was not feasible, but selected limited quantitative comparisons had been provided, and he briefly described these comparisons.

Dr. Rice then reviewed the charge questions that had been given to the SAB Panel. These questions focused on how EPA had addressed: 1) selecting key studies for further analyses; 2) pharmacokinetic modeling; 3) the noncancer assessment; 4) the cancer assessment; and 5) uncertainty analysis.

Dr. Buckley thanked Dr. Rice for his presentation. He stated that Panel members would have time to ask questions after public comments had been presented.

### *Public Comments*

The Chair stated that one hour had been reserved for public comments and he indicated that the Panel would hear comments from individuals who had previously asked to be placed on the list of public speakers<sup>6</sup>. He stated that speakers should limit their oral statements to three minutes. The following speakers provided oral statements.

Lesa Aylward, Summit Toxicology, provided comments on behalf of the American Chemistry Council. Her comments focused on the need to consider several additional points in the charge to be addressed by the SAB Dioxin Review Panel.<sup>7</sup>

Jay Silkworth, General Electric Company, commented that SAB Panel should carefully consider new research information that was not thoroughly evaluated in the EPA's current Dioxin Reanalysis.<sup>8</sup>

Joshua Cohen, Tufts University Medical Center, provided comments on EPA's treatment of uncertainty in the dioxin document to be reviewed by the Panel. He commented that additional work was needed in the treatment of uncertainty.

Russell Kenan, Integral Consulting, provided comments on behalf of the American Chemistry Council. He commented that that the Panel should consider whether EPA had consistently and appropriately followed its own guidelines and principles and applied a weight of evidence approach, using best available scientific information, in its evaluation of dioxin toxicity and risk.<sup>9</sup>

Donald Hassig, Cancer Action Network. Mr. Hassig's comments focused on the need for EPA to publish a final dioxin reassessment without further delay.<sup>10, 11</sup>

Maureen Swanson, Learning Disability Association of America, commented on the association between dioxin exposure and learning and developmental disabilities. She urged release of the dioxin reassessment without further delay.

Mike Schade, Center for Health, Environment and Justice. Anjolie Bains, speaking for Mr. Schade, expressed support for characterization of dioxin as a carcinogen. She commented that there was no need for further delay in completing the dioxin assessment and indicated that it should be finalized without delay.

Joyce Martin, American Association on Intellectual and Developmental Disabilities, commented on the association between dioxin exposure, birth defects, and intellectual disabilities. She commented that delay in releasing the dioxin assessment would have an impact upon children's health and urged completion of the review and release of the report as soon as possible.

Robert Spiegel, Edison Wetlands Association. Eric Galbietti, speaking for Robert Spiegel commented that he was extremely concerned about dioxin exposure at a number of contaminated sites. He commented that dioxin had been detected at levels of concern at these sites and that it needed to be regulated. He expressed support for classification of dioxin as a carcinogen and asked that the SAB expedite its review of the dioxin document.

David Fischer, American Chemistry Council, commented on the public review process for EPA's dioxin document. He commented on the need for greater opportunity for public input.<sup>12</sup> He stated that there had been little time for the public to comment on EPA's document and noted that he was pleased that the SAB would hold a second face-to-face meeting for its review after the close of public comment period.

Ryan Black, Coastal Conservation League, commented on global air quality threats posed by dioxin. He expressed support for characterization of dioxin as a carcinogen and stated that EPA should complete its dioxin assessment as soon as possible.

Katie Huffling, Alliance of Nurses for Healthy Environments, commented on the linkage between dioxin exposure and cancer and other disabilities. She commented on need to have food, air, and water that is free of dioxin and urged EPA to complete the dioxin assessment without further delay.

Todd Abel, Chlorine Chemistry Division, of the American Chemistry Council, commented on EPA's dioxin reanalysis as it related to the NAS recommendations, and suggested some additional charge questions for the Panel's consideration.<sup>13</sup>

Judy Levin, Center for Environmental Health, commented that incineration of medical waste was a source of dioxin and stated that there were no safe levels of dioxin. She expressed support for characterization of dioxin as a carcinogen. She commented that the delay in EPA's dioxin assessment had resulted in additional exposure to dioxin and urged EPA to complete the assessment.

Sarah Westervelt, Basel Action Network, stated that her organization worked on the issue of toxic electronic waste. She commented on how dioxin is generated from incineration of waste material. She encouraged EPA to release the dioxin assessment and indicated that it was long overdue.

Rick Hind, Greenpeace, commented on the importance of completing the dioxin assessment without further delay. He commented on the sources of dioxin and its dispersal in the environment, and urged the Panel help EPA move ahead to complete the assessment.

The Chair thanked the speakers for their comments. A caller requested the opportunity to provide additional comments, however the Chair indicated that additional time was not available to hear comments from speakers who had not previously registered to provide oral statements. The Chair stated that he wanted to move to the next item on the agenda. He then called for questions from the Panel on EPA's draft document, and discussion of the charge and agenda for the upcoming Panel meeting.

*Clarifying questions concerning EPA's presentation, the charge, and agenda for the July 13-15 meeting*

The Chair asked Panel members whether they had questions for EPA on the draft dioxin document or the charge to the Panel.

A member asked EPA staff to clarify when whole blood, plasma, and whole weight concentrations of dioxin had been used for the analyses. EPA staff responded that whole blood concentrations had been used for the primary analyses.

The member asked EPA staff to clarify how they had defined primary analyses. EPA staff responded that the primary analyses were derivation of the reference dose (RfD) and oral cancer slope factor.

A member asked EPA staff to clarify how doses had been approached for the RfD determination. EPA staff responded that two studies had been designated as co-principal. In the first study, Baccarelli et al., 2008 (cited in the EPA document, *Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*) EPA considered elevated thyroid stimulating hormone (TSH) and used the Emond physiologically based pharmacokinetic (PBPK) model to look at relevant blood concentration. In the second study, Mocarelli et al., 2008 (cited in the document, *EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments*) EPA looked at decreased sperm production. TCDD dose was determined by averaging the lifetime doses associated with peak exposure and a maximum 10 year exposure window.

A member asked whether EPA had assumed that doses could be calculated by extrapolating from lipid to blood. EPA staff responded that the Agency had just looked

at blood data. A member asked whether EPA had considered only TCDD levels. EPA staff responded that they had looked only at TCDD levels.

A member asked EPA to clarify the statement that benchmark dose modeling was difficult. EPA staff responded that there were many data sets that were not amenable to benchmark modeling.

A member asked EPA staff to elaborate on limitations that precluded making strong conclusions based on the nonlinear dose-response modeling exercises. EPA responded that Table 5-20 of the draft dioxin document presented candidate points of departure and reference doses for TCDD carcinogenicity based on combined tumor responses from animal bioassays. Staff noted that Table 5-21 provided illustrative RfDs based on representative endpoints for hypothesized events following AhR activation for TCDD-induced liver tumors. EPA staff pointed out data limitations (in section 5.2.4.1.5.2.3 of EPA's document) that prevented drawing strong conclusions.

A member asked EPA staff whether there was any concern about lactational exposure in the Baccarelli (2008) study. EPA staff responded that measurements had been taken "a couple of days after birth."

#### *Discussion of upcoming face-to-face meeting*

The Chair reviewed the agenda and work to be completed in preparation for the upcoming July 13-15 meeting of the Panel. He noted that each member had been assigned as a lead discussant for charge questions corresponding to sections of EPA's draft document. He stated that at the face-to-face meeting the Panel would have time to discuss the issues to be addressed in response to the questions. He noted that the Panel would have a second meeting to work toward developing a consensus on the response to the charge questions.

Several Panel members commented on the length of EPA's document and the amount of material to be reviewed and noted that they might have additional questions for EPA at the face-to-face meeting. Members asked whether EPA would respond to questions from the Panel at the upcoming meeting. The Chair responded that EPA staff would answer clarifying questions and provide additional information in response to questions. A member asked whether the Panel would meet in subgroups at the upcoming meeting. The Chair responded that the Panel would meet in plenary session for the entire meeting and not break into subgroups.

The Chair called for additional questions from the Panel. Members had no additional questions so the Chair asked the DFO whether there were any other items to discuss before adjourning. The DFO stated that if members had no additional questions there were no other items on the agenda. He thanked the members of the Panel and public for calling and adjourned the teleconference.

Respectfully Submitted:

Certified as True:

*/Signed/*

*/Signed/*

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Dr. Thomas Armitage  
Designated Federal Officer

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Dr. Timothy Buckley, Chair  
SAB Dioxin Review Panel

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by Panel members during the course of deliberations within the meeting. Such ideas, suggestions and deliberations do not necessarily reflect consensus advice from Panel members. The reader is cautioned to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, commentaries, letters or reports prepared and transmitted to the EPA Administrator following the public meetings.

## ATTACHMENT A: PANEL ROSTER

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### U.S. Environmental Protection Agency Science Advisory Board Dioxin Review Panel

#### CHAIR

**Dr. Timothy Buckley**, Associate Professor and Chair, Division of Environmental Health Sciences, College of Public Health, The Ohio State University, Columbus, OH

#### MEMBERS

**Dr. Harvey Clewell**, Director of the Center for Human Health Assessment, The Hamner Institutes for Health Sciences, Research Triangle Park, NC

**Dr. Louis Anthony (Tony) Cox, Jr.**, President, Cox Associates, Denver, CO

**Dr. Elaine Faustman**, Professor, Department of Environmental and Occupational Health Sciences, School of Public Health and Community Medicine, University of Washington, Seattle, WA

**Dr. Scott Ferson**, Senior Scientist, Applied Biomathematics, Setauket, NY

**Dr. Jeffrey Fisher**, Research Toxicologist, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR

**Dr. Helen Håkansson**, Professor of Toxicology, Unit of Environmental Health Risk Assessment, Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden

**Dr. Russ Hauser**, Frederick Lee Hisaw Professor, Department of Environmental Health, Harvard School of Public Health, Boston, MA

**Dr. B. Paige Lawrence**, Associate Professor, Departments of Environmental Medicine and Microbiology and Immunology, School of Medicine and Dentistry, University of Rochester School of Medicine and Dentistry, Rochester, NY

**Dr. Michael I. Luster**, Independent Consultant, Morgantown, WV

**Dr. Paolo Mocarelli**, Professor of Clinical Biochemistry, Department of Clinical Laboratory, Hospital of Desio-Nuovo Monoblous, University of Milano Bicocca, 20033 Desio-Milano, Italy

**Dr. Victoria Persky**, Professor, Epidemiology and Biostatistics Program, School of Public Health, University of Illinois at Chicago, Chicago, IL

**Dr. Sandra L. Petersen**, Professor, Associate Graduate Dean, Department of Veterinary and Animal Sciences, College of Natural Sciences, University of Massachusetts-Amherst, Amherst, MA

**Dr. Karl Rozman**, Professor, Pharmacology, Toxicology and Therapeutics, The University of Kansas Medical Center, Kansas City, KS

**Dr. Arnold Schecter**, Professor, Environmental and Occupational Health Sciences, School of Public Health-Dallas Campus, University of Texas, Dallas, TX

**Dr. Allen E. Silverstone**, Professor, Department of Microbiology and Immunology, Health Science Center, SUNY Upstate Medical University, Syracuse, NY and Adjunct Professor of Environmental Medicine, University of Rochester School of Medicine and Dentistry, Rochester, NY.

**Dr. Mitchell J. Small**, The H. John Heinz III Professor of Environmental Engineering, Department of Civil & Environmental Engineering and Engineering & Public Policy, Carnegie Mellon University, Pittsburgh, PA

**Dr. Anne Sweeney**, Professor of Epidemiology, Department of Epidemiology and Biostatistics, School of Rural Public Health, Texas A&M Health Science Center, College Station, TX

**Dr. Mary K. Walker**, Professor, Division of Pharmaceutical Sciences, College of Pharmacy, University of New Mexico, Albuquerque, NM

#### **SCIENCE ADVISORY BOARD STAFF**

**Dr. Thomas Armitage**, Designated Federal Officer, U.S. Environmental Protection Agency, Washington, DC

## Materials Cited

The following meeting materials are available on the SAB Dioxin Review Panel Web site, at the June 24, 2010 Meeting Page

<http://yosemite.epa.gov/sab/sabproduct.nsf/MeetingCal/3EEF9488F3BE50E2852577120059D3D7?OpenDocument>

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<sup>1</sup> Federal Register Notice Announcing the Meeting

<sup>2</sup> Agenda for the June 8, 2010 teleconference

<sup>3</sup> Charge to the Panel

<sup>4</sup> Agency Briefing Material - Presentation: EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments

<sup>5</sup> Dioxin Reassessment - Response to the National Academies of Science - EPA's Reanalysis of Key Issues Related to Dioxin Toxicity (main text and appendices)

<sup>6</sup> SAB Staff Office Material - List of Public Speakers

<sup>7</sup> Public Comments Submitted to the SAB Staff Office - Public Comments From Lesa Aylward on Behalf of the American Chemistry Council

<sup>8</sup> Public Comments Submitted to the SAB Staff Office - Public Comments From Jay Silkworth, General Electric Company

<sup>9</sup> Public Comments Submitted to the SAB Staff Office - Public Comments From Russell Keenan on behalf of the American Chemistry Council

<sup>10</sup> Public Comments Submitted to the SAB Staff Office - Public Comments From Donald L. Hassig, Cancer Action NY, Report Titled: *Disinformation Cancer Epidemic: A Record...*

<sup>11</sup> Public Comments Submitted to the SAB Staff Office - Public Comments From Donald L. Hassig, Cancer Action NY, Three Papers Submitted June 23, 2010

<sup>12</sup> Public Comments Submitted to the SAB Staff Office – Public Comments From David B. Fischer on Behalf of the American Chemistry Council

<sup>13</sup> Public Comments Submitted to the SAB Staff Office – Public Comments From Todd Abel on Behalf of the Chlorine Chemistry Division of the American Chemistry Council