U.S. Environmental Protection Agency (U.S. EPA)
National Center for Environmental Assessment (NCEA)
State-of-the-Science Workshop to Discuss Issues Relevant for Assessing the Health Hazards of Formaldehyde Inhalation

April 30th to May 1st, 2014
Crystal City Marriott at Reagan National Airport
(1999 Jefferson Davis Highway, Arlington, VA)

Final Agenda

Wednesday, April 30, 2014

8:00 am On-site registration

8:30 am Welcome and introduction to issues
Kenneth Olden, U.S. EPA NCEA Director

9:00 am Session 1. Interactions of inhaled formaldehyde at the portal of entry: toxicokinetics and comparisons to endogenous formaldehyde

9:00-9:15 *Introduction:*

Ravi Subramaniam, U.S. EPA NCEA, session chair
Mel Andersen, The Hamner Institutes for Health Sciences, session chair

9:15-10:30 *Speaker presentations:*
[15-20 minute talks, with up to 5 minutes each for direct, clarifying questions]

Dean Appling, University of Texas at Austin
James Swenberg, University of North Carolina at Chapel Hill
Lisa Peterson, University of Minnesota

10:30-10:45 *Break*

10:45-12:15 *Discussion (speakers, discussants, and audience):*
[3-5 minute commentary per topic per discussant, with 1 hour for follow-up discussion and audience questions]

Paul Schlosser, U.S. EPA NCEA, discussant
Martyn Smith, University of California at Berkeley, discussant
Jeff Ross, U.S. EPA National Health and Environmental Effects Research Laboratory, discussant

1) What are the likely similarities and differences in the toxicokinetics of inhaled and endogenous formaldehyde? To what degree, and in what form, is endogenously produced formaldehyde available to react with cellular macromolecules in various tissue compartments? ~~What are the implications of these~~How does current knowledge of the similarities and differences in these two forms of formaldehyde

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affect y~~for~~ our understanding of formaldehyde toxicity/carcinogenicity?

2) What evidence is available concerning levels of endogenous formaldehyde measured in various tissues, including blood, and what are the uncertainties? ~~Regarding measurements differentiating between exogenous and endogenous DNA monoadducts induced by formaldehyde, are there any relevant uncertainties and what~~ How can these measures of endogenous and exogenous formaldehyde ~~is the potential use of these measurements as internal dose metrics~~assist in selecting dose metrics for formaldehyde risk assessments? ~~To what extent, if any, would uncertainties regarding measurements of formaldehyde and formaldehyde adducts be expected to affect interpretation of comparisons between endogenous levels and the internal dose due to exogenous exposure?~~

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12:15 pm Lunch (on your own)

1:15 pm Case Study. Bounding cancer risk estimates using measurements of endogenous formaldehyde

1:15-1:20 *Introduction:*

Conference moderator, ICF International

1:20-1:50 *Speaker presentations:*
[10-15 minute talks, with up to 5 minutes each for direct, clarifying questions]

Thomas Starr, TBS Associates
Kenny Crump, Independent consultant

1:50-2:15 *Discussion (speakers, workshop participants, and audience)*

2:15 pm Session 2. Mechanistic evidence for lymphohematopoietic (LHP) cancers following formaldehyde exposure

2:15-2:30 *Introduction:*

Andrew Kraft, U.S. EPA NCEA, session chair
Lorenz Rhomberg, Gradient Corporation, session chair

2:30-3:45 *Speaker presentations:*
[15-20 minute talks, with up to 5 minutes each for direct, clarifying questions]

David Eastmond, University of California at Riverside
Bernard Goldstein, University of Pittsburgh
Richard Albertini, University of Vermont

3:45-4:00 *Break*

4:00-5:30 *Discussion (speakers, discussants, and audience):*
[3-5 minute commentary per topic per discussant, with 1 hour for follow-up

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discussion and audience questions]

Luoping Zhang, University of California at Berkeley, discussant
Robert Snyder, Rutgers University (retired), discussant
Martha Sandy, California EPA, discussant

1) What mechanistic events that have been associated with the pathogenesis of LHP cancers following environmental exposures other than formaldehyde may be relevant to formaldehyde-mediated effects? Does formaldehyde need to be systemically distributed to affect the incidence of LHPs? What evidence is available to inform whether potential mechanistic pathways may be differentially affected due to different patterns of exposure (e.g., exposure frequency, duration, or levels)? Are there any data available to support or not support these hypotheses?

2) What questions and uncertainties remain, and is there specific research that could address these unknowns?

5:30 pm Adjourn

Thursday, May 1, 2014

8:30 am On-site registration

9:00 am Session 3. Review of the epidemiologic evidence on LHP cancers

9:00-9:15 *Introduction:*

Barbara Glenn, U.S. EPA NCEA, session chair
Jim Collins, Dow Chemical Company, session chair

9:15-10:55 *Speaker presentations:*
[15-20 minute talks, with up to 5 minutes each for direct, clarifying questions]

Patricia Stewart, Independent consultant
Anneclaire De Roos, Drexel University
Harvey Checkoway, University of California at San Diego
Thomas Bateson, U.S. EPA NCEA

10:55-11:10 *Break*

11:10-12:30 *Discussion (speakers, discussants, and audience):*
[3-5 minute commentary per topic per discussant, with 1 hour for follow-up discussion and audience questions]

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Laura Beane-Freeman, National Cancer Institute, discussant
Leslie Stayner, University of Illinois at Chicago, discussant
Karen Robinson, Johns Hopkins University, discussant

1) How might the specific exposure settings and metrics used in the occupational studies of formaldehyde exposure and cancer mortality, and their associated uncertainties, affect interpretations of study results? What are the uncertainties in the available outcome definitions for LHP cancer mortality, including the potential for misclassification, and how might these uncertainties influence interpretations? What are the tradeoffs between analyses focused on broad versus more specific LHP diagnostic categories or exposure assessments?

2) Two approaches to the systematic review of evidence on the potential association of formaldehyde inhalation with LHP cancer mortality will be presented. What are the key advantages and disadvantages of the two presented approaches for evaluating the epidemiologic evidence? Are there additional considerations for weighing the epidemiologic evidence that have not been presented?

12:30 pm Lunch (on your own)

1:30 pm Wrap-Up. Perspectives on the application of information discussed at the workshop to assessing the potential LHP cancer hazard(s) of inhaled formaldehyde.

1:30-1:40 *Introduction:*

Vincent Cogliano, U.S. EPA NCEA, session chair

1:40-2:20 *Discussant perspectives:*
[5 minutes per discussant, each with some time for direct, clarifying questions]

Mel Andersen, The Hamner Institutes for Health Sciences [session 1 chair]
Lorenz Rhomberg, Gradient Corporation [session 2 chair]
Jim Collins, Dow Chemical [session 3 chair]
David Eastmond, University of California at Riverside [session 2 speaker]
Martha Sandy, California EPA [session 2 discussant]
Leslie Stayner, University of Illinois at Chicago [session 3 discussant]

1) In your opinion, what were the most important 1-3 points discussed at the workshop to inform the potential for formaldehyde to cause LHP cancers, and why?

2) What are the key uncertainties you believe remain regarding the data available on formaldehyde and LHP cancers, and how do you think those uncertainties should affect hazard identification?

2:20-2:35 *Participant discussion (session chair and discussants)*

2:35-3:00 *Audience discussion (session chair, discussants, and audience)*

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3:00 pm Adjourn