

**Summary Minutes of the
U.S. Environmental Protection Agency
Trichloroethylene Review Panel
Public Teleconference
September 13, 2010
12:00 – 4:00 pm, Eastern Time**

TCE Panel:

Dr. Deborah Cory-Slechta
Dr. Scott Bartell
Dr. Aaron Blair
Dr. Anneclaire De Roos
Dr. Rodney Dietert
Dr. Claude Emond
Dr. Montserrat Fuentes
Dr. David G. Hoel
Dr. Gunnar Johanson
Dr. Michael Pennell
Dr. Kenneth Portier
Dr. Gloria Post
Dr. Gary Rankin
Dr. Ivan Rusyn
Dr. Ornella Selmin
Dr. Brian Thrall
Dr. John Vena
Dr. Virginia Weaver

Purpose:

To discuss the Panel's draft report on the review of EPA's IRIS Toxicological Review of Trichloroethylene (October 2009).

Designated

Federal Officer:

Dr. Holly Stallworth, Designated Federal Officer

Other EPA Staff:

Weihshueh Chiu, Susan Makris, Becki Clark, Cheryl Siegel Scott, Kathryn Z. Guyton, Ambuja Bale, Maureen Gwinn, Rebecca Dzubow, Stan Barone, Weihshueh Chiu, Jennifer Jinot, Dave Bussard, Linda Cooper, Jane Caldwell, Allen Marcus, Norman Birchfield

Public:

Paul Dugard, Halogenated Solvents Industry Alliance
Catherine Kurts, Navy Public Health
Resha Putzrath, Navy Public Health
Amanda Ross, ICF
David Dodge, Gradient Corporation
Linda Wilson, NY State Attorney General's Office

Kofi Asante, D.C. Dept. of Environment
Paul Dugard, Halogenated Solvents Industry Association
W. Caffey Norman III, Patton Boggs LLC

Webpage: The meeting agenda, public comments and draft report are all posted at:

<http://yosemite.epa.gov/sab/sabproduct.nsf/a84bfee16cc358ad85256ccd006b0b4b/8c9fba5434d4a21585257766004cb703!OpenDocument&Date=2010-09-13>

Meeting Summary

The discussion followed the issues, as presented in the meeting agenda.

MONDAY, SEPTEMBER 13, 2010

Opening of Public Meeting

Dr. Stallworth convened the meeting and explained that Science Advisory Board operates under the Federal Advisory Committee Act.

Dr. Paul Dugard of the Halogenated Solvents Industry Association (HSIA) called on the Panel to recommend that the Lash estimate of s-dichlorovinyl glutathione (DCVG) production be dropped from practical consideration. Dr. Dugard also criticized the cancer slope factors based on the Charbotel (2005) epidemiology study because of flaws in the exposure assessment.

Although they had registered to provide public comments, neither Mike Partain (breast cancer survivor) nor Ryan Livengood (LSI Corporation) were present on the teleconference.

Dr. Weihsueh Chiu reviewed NCEA's comments (posted at the above URL) on the Panel's draft Advisory. With respect to TCE-induced kidney tumors, Dr. Chiu asked the Panel to clarify its comments regarding one or more Modes of Action (MOA) that may be operative for TCE-induced kidney tumors. Dr. Chiu also asked the Panel to clarify which Lash study is being compared to Green et al (1997a) as well as statements about data from the Green et al (1997a) study. Dr. Chiu asked the Panel for references to assist EPA in comparing analytical methodologies used to estimate DCVG formation. The Panel subgroup did not have specific recommendations on references.

One of the panelists explained that the Panel was concerned about possible overestimation resulting from EPA taking an average for DCVG formation, averaging together 2 studies. Since rats are more susceptible than mice to renal cancer, then the Green study was more reflective. Analytical method using radioactive chemical is generally more accurate than spectrometric analysis of metabolites. One panel member mentioned Lash et al. (1998) (in Drug Metab Dispos 26: 12-19) indicated that rats are

more susceptible to renal cancer than mice. The Panel agreed EPA did not conclude TCE-induced kidney tumors were mediated solely by a mutagenic MOA, and that “solely” should be deleted in the sentence

It was suggested that EPA should strengthen the discussion of how each of the in vitro and in vivo data sets were used to estimate DCVG estimates formation and the need to acknowledge potential limitations of the methodologies used.

With respect to non-cancer and cancer effects on the lung, one panelist clarified that the IRIS assessment's discussion of lung effects could be expanded to underscore its importance. With respect to toxicokinetic variability (charge question 7), one panelist said that “toxicokinetic variability can be adequately quantified using existing data” was a statement in the charge question with which the Panel disagreed. This panelist noted that this particular statement was not in the IRIS assessment.

With respect to the variability between animals and whether it was adequately captured in the modeling, panelists decided to delete draft text suggesting that the IRIS assessment assumed variability is captured in the prior distributions for model parameters.

On the topic of meta-analysis of cancer epidemiology (charge question 2), the Panel acknowledged that information on the relative risk selection and confidence intervals are explained in Appendix C. In response to Dr. Chiu's comments on the table on kidney cancer on p. 14 of the draft Advisory, panelist decided to delete the table and instead provide text that stressed the need to make assumptions about lags and confidence intervals transparent. Panelist also agreed to substitute the word “appropriate” for “conservative” to describe the approach of choosing highest quality studies.

Panelists discussed the need for EPA to be clear about using the entire cohort or the TCE sub-cohort. Panelists noted that liver toxicity and carcinogenesis in the mouse should not be completely ignored. Panelists also responded to Dr. Chiu's questions about the Advisory's statements on role of the liver as a target tissue being underemphasized in the IRIS assessment.

In response to Dr. Chiu's question about the draft Advisory's language on PPAR α agonism and its sequelae being key events in TCE-induced human liver carcinogenesis, Panelists talked about the differences between human liver cancers and mouse liver cancers. One Panelist agreed to add text suggesting that particular tumors may or may not be dependent on PPAR α agonism. Panelists discussed how common forms of human cancer are not the same and that PPAR α agonism does not lead to peroxisome proliferation. Panelists agreed that activation of PPAR α is an important but not limiting factor for the development of mouse liver tumors.

Dr. Cory-Slechta then walked the Panel through responses to charge questions. Minor edits were suggested in several places throughout the responses to charge questions as well as in the letter to the Administrator. Panelist agreed to delete the recommendation that said EPA should provide a more balanced description of the TCE's adverse health

effects on both kidney and liver. Panelists also agreed to delete a sentence in the letter to the Administrator that said EPA should take into consider the uncertainties associated with possible confounding exposure to cutting oils.

Before adjourning the teleconference, Dr. Stallworth asked that lead discussants provide revised text within 10 days to incorporate the points discussed in the teleconference.

On Behalf of the Committee,
Respectfully Submitted,

Holly Stallworth, Ph.D. /s/
Designated Federal Officer

Certified as True:

Deborah Cory-Slechta, Ph.D./s/
Chair, SAB Trichloroethylene Review Panel

NOTE AND DISCLAIMER: The minutes of this public meeting reflect diverse ideas and suggestions offered by committee members during the course of deliberations within the meeting. Such ideas, suggestions, and deliberations do not necessarily reflect definitive consensus advice from the panel members. The reader is cautioned to not rely on the minutes 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.