



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

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THE ADMINISTRATOR

Deborah L. Swackhammer, Ph.D.
Chairwoman
Science Advisory Board
Deborah Cory-Slechta, Ph.D.
Chairwoman
Trichloroethylene Review Panel
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Dr. Swackhammer and Dr. Cory-Slechta:

Thank you for your January 11, 2011, report on the U. S. Environmental Protection Agency's draft assessment, "Toxicological Review of Trichloroethylene." As you know, trichloroethylene is a chemical of great importance to the EPA and its stakeholders, and the database on trichloroethylene's health effects is extensive with difficult scientific issues. Please know that we are grateful for the time, effort and thought you invested in the Trichloroethylene Review Panel's independent expert peer review and your efficiency in conducting it.

I am very pleased to recognize the panel's thorough consideration of the many important science issues in the TCE assessment and the care taken with the Science Advisory Board's advice. It is extremely valuable for the EPA to know that the panel supports the agency's scientific approaches and conclusions on the hazard characterization and dose-response assessment of TCE.

Overall, the panel: (1) supported the use of the agency's updated PBPK model for trichloroethylene; (2) found that the agency adequately synthesized the available scientific information on TCE non-cancer toxicity; (3) determined that the agency's meta-analyses for kidney cancer, lymphoma and liver cancer were well-conducted; (4) agreed with the agency's conclusion that TCE is carcinogenic to humans by all routes of exposure; (5) agreed that a mutagenic mode of action is operative for TCE-induced kidney tumorigenesis; and (6) supported the agency's approaches for deriving a reference concentration and reference dose for non-cancer effects, and an inhalation unit risk and oral slope factor for carcinogenic effects.

I especially appreciated the SAB's commendation of the EPA for its comprehensive approach and responsiveness to the National Academy of Sciences recommendations.

The panel also offered recommendations that will enhance the transparency of the draft assessment and strengthen the scientific basis for the conclusions presented. These include: (1) suggestions for better documenting the PBPK model; (2) selecting the immunological and cardiac malformation endpoints as the primary basis for the RfC and RfD while using the candidate RfC/RfDs for kidney effects as supporting values; (3) noting that evidence also supports, in addition to mutagenic MOA, MOAs involving cell death and compensatory cell proliferation for TCE-induced kidney tumorigenesis; and (4) including a discussion of assumptions used in the dose-response analysis for carcinogenic effects.

The EPA is already addressing the SAB's recommendations. We intend to work expeditiously to complete this toxicological review and post it in the Integrated Risk Information System.

In the meantime, I thank you once more for your insightful comments and for your timely review.

Sincerely,

A handwritten signature in blue ink, appearing to read 'Lisa P. Jackson', with a stylized, flowing script.

Lisa P. Jackson

A handwritten note in blue ink that says 'Thank you!' with a large exclamation point.