



THE ADMINISTRATOR OF THE ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OCT 08 2015

Peter S. Thorne, Ph.D.
Chairman
Science Advisory Board
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Dear Dr. Thorne:

Thank you for your August 7, 2015, letter in which you provided the Science Advisory Board review panel's comments on the U.S. Environmental Protection Agency's draft "Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide" that was developed through the Integrated Risk Information System program and released for external peer review in August 2014.

As you know, the SAB in 2007 peer reviewed an earlier version of the draft assessment. It was revised in response to the SAB's recommendations, and, primarily due to additional modeling of the epidemiologic data, the EPA requested an additional SAB peer review.

We appreciate the panel's thorough review and constructive recommendations. We are particularly grateful that the SAB found the 2014 revised draft assessment to be highly responsive to both the 2007 SAB recommendations and to the public comments.

We also are pleased that the SAB agreed with key decisions in the draft assessment, including the following:

- the characterization of EtO as "carcinogenic to humans";
- the conclusion that the National Institute of Occupational Safety and Health dataset remains the most appropriate dataset for dose-response analysis;
- recognition of a period of latency for the development of cancer;
- the use of a two-piece spline model for estimating breast cancer incidence; and
- support for the low-dose extrapolation methodology used and the lack of a scientific basis for estimating cancer risk from EtO exposure using nonlinear extrapolation methods.

Your letter also included several recommendations from the SAB that will enhance the clarity of the EPA's assessment and strengthen the scientific basis for its conclusions. The EPA will carefully consider the SAB's report and make revisions to the assessment that address these recommendations. Some of the key SAB recommendations that we will address include:

- improving the considerations used for model selection for breast cancer incidence, including less reliance on the Akaike information criterion;
- further considering exposure-response models for lymphoid cancer that use continuous individual-level exposure data and updating the justification for model selection;
- presenting sensitivity analyses in terms of unit risk estimates;

- adding descriptive summaries of the characteristics of the NIOSH cohort and its exposures; and
- further consideration of the Mikoczy et al. (2011) study of Swedish sterilization workers.

The EPA appreciates the SAB statement that the advice and recommendations in the report can likely be addressed quickly and that the draft assessment should move forward to be finalized. We intend to finalize the assessment as expeditiously as possible.

I want to convey once more my gratitude for the SAB and its Chemical Assessment Advisory Committee's thoughtful review of the EPA's draft IRIS carcinogenicity assessment of EtO. The SAB's contributions are extremely valuable to ensuring that the EPA uses the best available science in finalizing this important health assessment.

Sincerely,



Gina McCarthy