



January 26, 2024

Submitted via California ARB Comments Portal

California Air Resources Board  
Scientific Review Panel on Toxic Air Contaminants  
1001 I Street  
Sacramento, California 95812

Re: ACC Comments on Draft Cancer Inhalation Unit Risk Factor (IUR) for Ethylene Oxide

Members of the Scientific Review Panel:

The Ethylene Oxide Panel (EO Panel) of the American Chemistry Council (ACC) appreciates the opportunity to provide comments to the Scientific Review Panel (SRP) on OEHHA's proposed Cancer Inhalation Unit Risk Factor for ethylene oxide (EtO) and its accompanying Draft Technical Support Document (Draft IUR, 2023). The EO Panel includes the major producers and users of EO in North America.

These comments highlight key points related to the dose-response modeling and breast cancer that are discussed in greater detail in the attached ACC detailed comments on the Draft IUR that were submitted to OEHHA. As part of this review, we urge OEHHA to seriously consider our comments together with the more detailed ACC comments that address OEHHA's new analysis and evaluations. The attached ACC comments and slide presentation provide additional references and analysis supporting the following key points that summarize why dose-response analysis using a single log-linear CPH model has greater biological plausibility and is more consistent with the observed epidemiology data:

- The USEPA's 2-slope model is comprised of a steep slope in the low-dose region with high-dose plateau. This appears to be an artifact of embedded decisions made in the modeling, in particular:
  - o Combining men's & women's data exhibiting dramatically different exposure- response behaviors
  - o Incorrect statistics, misleading visual fit comparisons, over-reliance on biologically implausible log-cumulative models
- A steep slope in the low dose region is inconsistent with the epidemiology data.

- o Signals for LH, lymphoid and breast cancer are weak and inconsistent across available studies.
- A steep slope in the low-dose-region is inconsistent with the biological evidence
  - o Genotoxicity for EtO do not exhibit this behavior.
  - o EtO toxicokinetics do not exhibit the behavior of the EPA's steep initial slope.
  - o The carcinogenicity data for ethylene and EtO do not exhibit this behavior.
- EPA's 2-slope model overpredicts risk
  - o Overestimating cases in the range of observation.
  - o The resulting IUR predicts unacceptable excess risk in ambient air, exhaled air and fruits
  - o As such, the use of USEPA's IUR to assess, manage, and communicate risks from EtO is not recommended.
- The log-linear CPH model as performed by TCEQ is preferred
  - o Accurately predicts the number of cancer cases in range of observation for the NIOSH cohort.
  - o Is approximately linear in the low-dose range without exhibiting a plateau that is inconsistent with relevant mechanistic data.
  - o Is a standard model used for epidemiology and is more representative of the epidemiological weight of evidence.
  - o The behavior is consistent with the underlying genotoxicity, carcinogenicity and toxicokinetics of EtO.

We urge OEHHA to consider these comments and adopt an alternative such as the TCEQ approach. Thank you.

Sincerely,

*William Gulledge*

William Gulledge

Senior Director

Chemical Products & Technology Division

Attachments:

1. Comments to the California Air Resources Board Scientific Review Panel on Toxic Air Contaminants on the Draft OEHHA Inhalation Unit Risk, January 26, 2024
2. ACC Comments on Draft Cancer Inhalation Unit Risk Factor for Ethylene Oxide, June 14, 2023
3. American Chemistry Council Ethylene Oxide Panel Comments on the OEHHA Draft IUR, July 14, 2023