



The Ethylene Oxide Sterilization Association, Inc.

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July 29, 2026

Via OEHHA Portal

Dr. Rima Woods
Chief, Air Toxicology and Risk Assessment Section
Office of Environmental Health Hazard Assessment
1001 I Street, 12th Floor
Sacramento, CA 95814

Re: Draft Cancer Inhalation Unit Risk Factor for Ethylene Oxide

Dear Dr. Woods:

On behalf of its members, the Ethylene Oxide Sterilization Association, Inc. (EOSA) appreciates the opportunity to comment on the Office of Environmental Health Hazard Assessment's (OEHHA) draft Cancer Inhalation Unit Risk Factor (IUR) for ethylene oxide (EtO), and its accompanying Draft Technical Support Document (OEHHA Draft TSD Appendix B).

EOSA members represent a broad spectrum of the U.S. EtO sterilization industry. EOSA is a nonprofit organization that represents EtO suppliers, contract sterilizers, sterilization equipment manufacturers, medical device manufacturers, analytical equipment and systems suppliers, and laboratories. EOSA members work diligently to assist in providing life-saving sterile healthcare products around the world, more than 50 percent of which are sterilized using EtO. EOSA works to educate industry, regulators, and the public on the essential uses and benefits of EtO sterilization, for which no direct replacement is currently available, nor for the foreseeable future. EOSA also works to improve safety standards, foster industry communication, and provide a forum for many subjects related to EtO sterilization.

EOSA and its members believe that the safety of both communities surrounding EtO sterilization facilities and workers in the EtO sterilization industry is critically important. The EtO sterilization industry has historically undertaken, and will continue to undertake, significant efforts to reduce the emissions and potential worker exposure of EtO. EOSA is providing these comments to ensure that regulatory decisions reflect accurate facts, the best available science, and proven technologies and practices.

EOSA agrees with, and adopts by reference, the comments submitted by the American Chemistry Council (ACC) on the draft OEHHA IUR and TSD. As discussed in the ACC comments:

- OEHHA's draft IUR is based on incorrect visual "eyeballing" of continuous models with a few grouped categorical estimates which are not

the individual hazard rates that were modeled. OEHHA's primary rationale for rejecting the standard Cox proportional hazards model relies on a flawed comparison of relative-rate magnitudes, despite its own figures explicitly acknowledging that such visual comparisons are not an appropriate basis for interpretation.

- The unvalidated nature of the NIOSH exposure regression model introduces a high likelihood of exposure measurement error for >80% of the lymphoid and breast cancer cases exposed prior to 1978. Because the high-probability of exposure error impacts cases across the entire spectrum of cumulative exposures, any reliable IUR derivation must utilize models that incorporate the full spectrum of data rather than on low-dose segments that are driven by a small fraction of cases. Utilizing the entire dataset ensures greater statistical power and stabilizes risk estimates against the uncertainties inherent in the unvalidated NIOSH exposure model for the period prior to 1978, during which time no monitoring data were available.
- Recent molecular dosimetry and genotoxicity studies clarify this relationship at low exposure levels. These studies demonstrate that key mechanistic endpoints -- including systemic dosimetry measured as hemoglobin adducts, DNA adduct formation, mutations, and chromosomal damage -- do not exhibit a steep low-dose response. Instead, the biological response demonstrates (at most) a shallow linear response at low exposures, which steepens only at higher exposures possibly due to saturation of glutathione-dependent EtO detoxification depletion as well as possible saturation of DNA and cellular repair processes.
- DNA adduct, genotoxicity, toxicology, and pharmacokinetic evidence contradict all two-piece spline models or truncated linear models (*e.g.*, applied to a small subset of cases at lower exposures) featuring a biologically implausible steep low-dose slope based on a small subset of cases. Rather, the weight of scientific evidence, including data from the NIOSH studies, supports the opposite model shape, a shallow, single-slope linear dose-response model, such as a standard log-linear Cox proportional hazards (CPH) model.

In conclusion, the weight of scientific evidence demonstrates that OEHHA's draft risk assessment relies on a biologically untenable dose-response framework. A scientifically robust IUR must reject the implausibly steep low-dose slopes driven by a small fraction of cases. Furthermore, independent benchmarks -- including the genotoxicity studies, the UCC manufacturing cohort, modern molecular dosimetry, and empirical "reality checks" from heavily

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studied smoker cohorts -- stand in direct contradiction to deriving an exceptionally high inhalation IUR.

We urge OEHHA to correct its study quality criteria and evaluations, abandon incorrect and subjective visual fit comparisons, and align its final risk assessment with the overwhelming biological evidence that supports applying the standard log-linear CPH model to the NIOSH data. Given the lack of historical exposure data and major exposure reconstruction uncertainties within the NIOSH study, OEHHA should also derive an alternative IUR based on animal cancer bioassay data, which do not suffer from the exposure misclassification errors.

Thank you for your consideration of these comments. It is critical that OEHHA consider the information outlined in these comments, and the extensive comments provided by ACC. It is of paramount importance not to overestimate the potential risk of EtO from its critical sterilization use, and to be able to continue using this life sustaining, life-saving, and irreplaceable substance, to sterilize healthcare devices and pasteurize certain food products.

Sincerely,

A handwritten signature in black ink that reads "Meibao Zhuang". The script is fluid and cursive, with the first name "Meibao" and last name "Zhuang" clearly distinguishable.

Meibao Zhuang
Senior Manager
The Ethylene Oxide Sterilization Association, Inc.