Ethylene Oxide (EtO)

National Center for Environmental Assessment

October 29, 2018

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Summary of Key Points

- December 2016: IRIS EtO assessment released.
  - Inhaled EtO: "Carcinogenic to humans" and potency estimate is 50-fold higher than EPA estimate from 1985.
- August 2018: NATA update released.
  - Estimated cancer risks from inhaling EtO from several facilities exceeded 1 in 10,000.
  - Release of NATA raised the visibility of the IRIS EtO assessment.
- September 2018: Request for Correction submitted by ACC.

Background: Use and Exposure

- EtO is a gas used to sterilize and synthesize
- EtO at room temperature is a colorless, flammable gas.
- EtO is used:
  - In the synthesis of ethylene glycol and other industrial chemicals (> 99%).
  - To sterilize medical and dental equipment and other materials (< 1%).
- Human Exposures:
  - General population (off-site).
  - Workers (on-site).

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Regulatory Considerations

- EtO is a hazardous air pollutant (HAP) under the 1990 Clean Air Act.
- EtO's sterilization and fumigation uses are regulated by the Office of Pesticides Programs (OPP).

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Assessment History

- **During assessment development, two public comment periods and two SAB peer reviews were held:**
  - September 2006: Public comment period 1.
  - January 2007: First SAB peer review meeting.
  - July 2013: Public comment period 2.
  - November 2014: Second SAB peer review meeting.
  - June 2015: Quality Review by EPA chartered SAB
  - December 2016: Final IRIS assessment released.

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Assessment Scope

- Assessment evaluates the inhalation carcinogenicity of EtO and includes:
  - a cancer weight-of-evidence descriptor,
  - a MOA analysis,
  - an inhalation unit risk (IUR) estimate, and
  - dose-response information for occupational settings.
- Replaces a 1985 EPA Health Assessment Document.

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Cancer Hazard Characterization

- Carcinogenic to humans (by the inhalation route of exposure) based on:
  - Strong human evidence in EtO-exposed workers:
    - lymphohematopoietic cancers (males and females)
    - breast cancer (females)
  - Extensive animal evidence of carcinogenicity:
    - lymphohematopoietic cancers (rats and mice)
    - mammary carcinomas (mice)
  - Clear mechanistic evidence:
    - Strong evidence that EtO acts via a mutagenic mode of action.
- Implications of mutagenic mode of action:
  - Support for linear dose-response.
  - Support for increased susceptibility in children.

Dose-Response Analysis: Study selection

- Exposure-response models fit to data from a NIOSH study of sterilization workers. This study was selected because of:
  - High quality exposure estimates, large cohort size (17,530 workers from 13 sterilizing facilities), absence of co-exposures, and inclusion of women.
  - Both SAB panels concurred that NIOSH study was best single study for derivation of risk estimates.
- Union Carbide study was also considered, but had too many limitations compared to the NIOSH study, especially with regard to exposure assessment. Both SAB panels agreed with not using this study for generating risk estimates.

Dose-Response Analysis: Endpoint selection and modeling

- NIOSH study showed dose-response for lymphoid cancer (non-Hodgkin's lymphoma, myeloma and lymphocytic leukemia) and breast cancer.
- Results for lymphoid and breast cancer were combined.
- EPA selected the best-fitting continuous exposure model for estimating the IUR.
- Based on the best-fitting model, EPA estimates that breathing 1 ug/m3 for 70 years would result in a 5 in 1,000 cancer risk
  - In its 1985 assessment, EPA's IUR estimate was 50 times lower (less potent) and was based on animal instead of human data.

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What's next?

- Providing support to OAR and Regions on interpreting the assessment science and on risk communication
- September 2018: American Chemistry Council (ACC) submitted a Request for Correction to EPA
  - Scoping/planning meeting is being organized by OEI