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ETHYLENE OXIDE: AN UPDATE

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American Chemistry Council

ACC's Ethylene Oxide Panel

EO Panel Overview

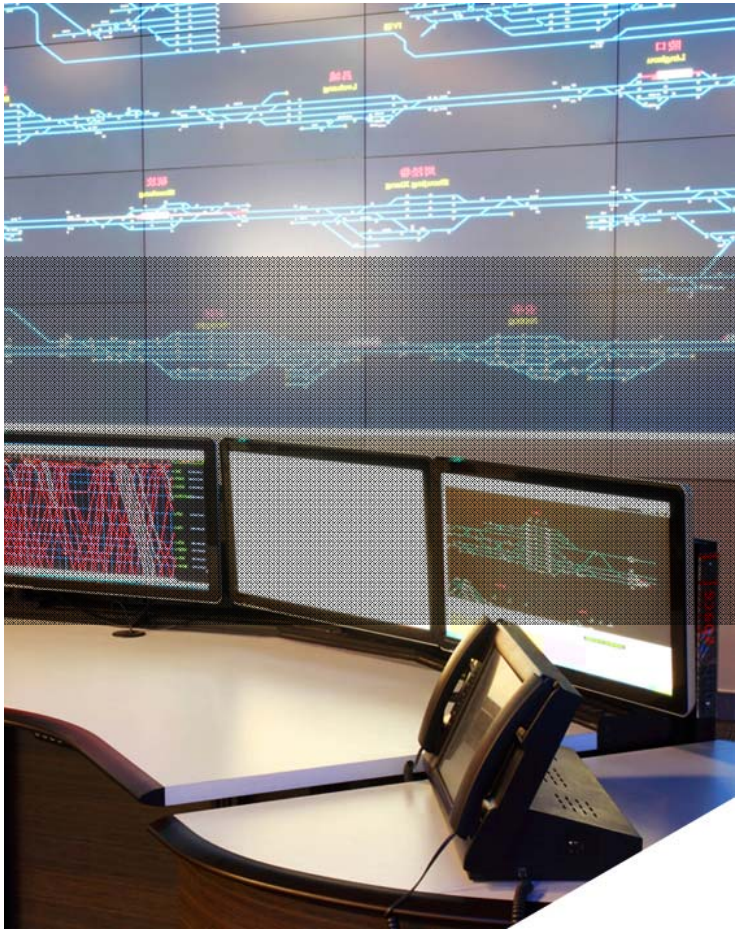
ACGIH TLV Review of EO

EPA Development of EO IRIS Assessment

Other Activities- EO Mode of Action

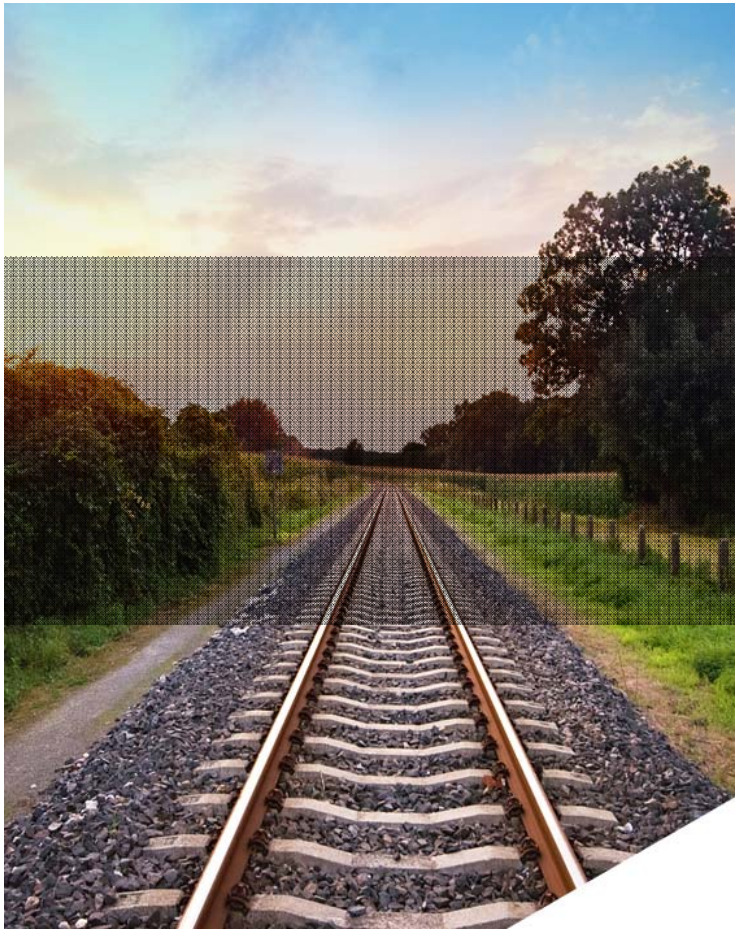
Ethylene Oxide

- Gas at Room Temperature
- Transported as a Liquid in Rail Cars; Also Transported Via Trucks
- Manufactured from Ethylene and Primarily Used as Chemical Intermediate (Production of Ethylene Glycol-Based Antifreeze and Other Chemicals)
- Sterilizing Agent for Medical Equipment
- IARC Classification- Group I Carcinogen



The EO Panel

- Includes Producers and Users of EO as Well as Sterilization- 13 Companies
- Part of the ACC's Ethylene Oxide/Ethylene Glycols Sector Group- Chemical Products & Technology
- Product Stewardship Commitment- EO Safety Task Group
- Product Stewardship Support- Toxicology Research Task Group



Other Activities

- **EO Product Stewardship Manual**

http://www.americanchemistry.com/ProductsTechnology/Ethylene-Oxide/EO-Product-Stewardship-Manual-3rd-edition/default.aspx

- **Incident and Information Exchanges**
- **Participation in ARASP**

ACGIH Review of the TLV

- **2011- TLV for EO Removed from the ACGIH Under Study List**
- **Current TLV Value: 1ppm**
- **Current ACGIH Notations: A2 (Suspected Human Carcinogen); No New Epidemiological Evidence to Support Moving to an A1 Classification**
- **TLV Basis: Cancer / CNS Impairment**

Justification for TLV Action

Despite the extensive investigations of EO worker cohorts, the results do not indicate a specific pattern for any type of cancer.

IARC recognized that this human data is also limited.

REACH Consortium (2010) concluded no cancer mortality is correlated with EO exposure to humans (based on low exposure in the workplace due to control measures).

EO IRIS Assessment

- Draft Proposed in 2006 with Public Comment Period
- SAB Review of Draft in 2007
- EPA Inhalation Carcinogenicity and Response to SAB Review- Dated July 2011 but Just Recently Posted

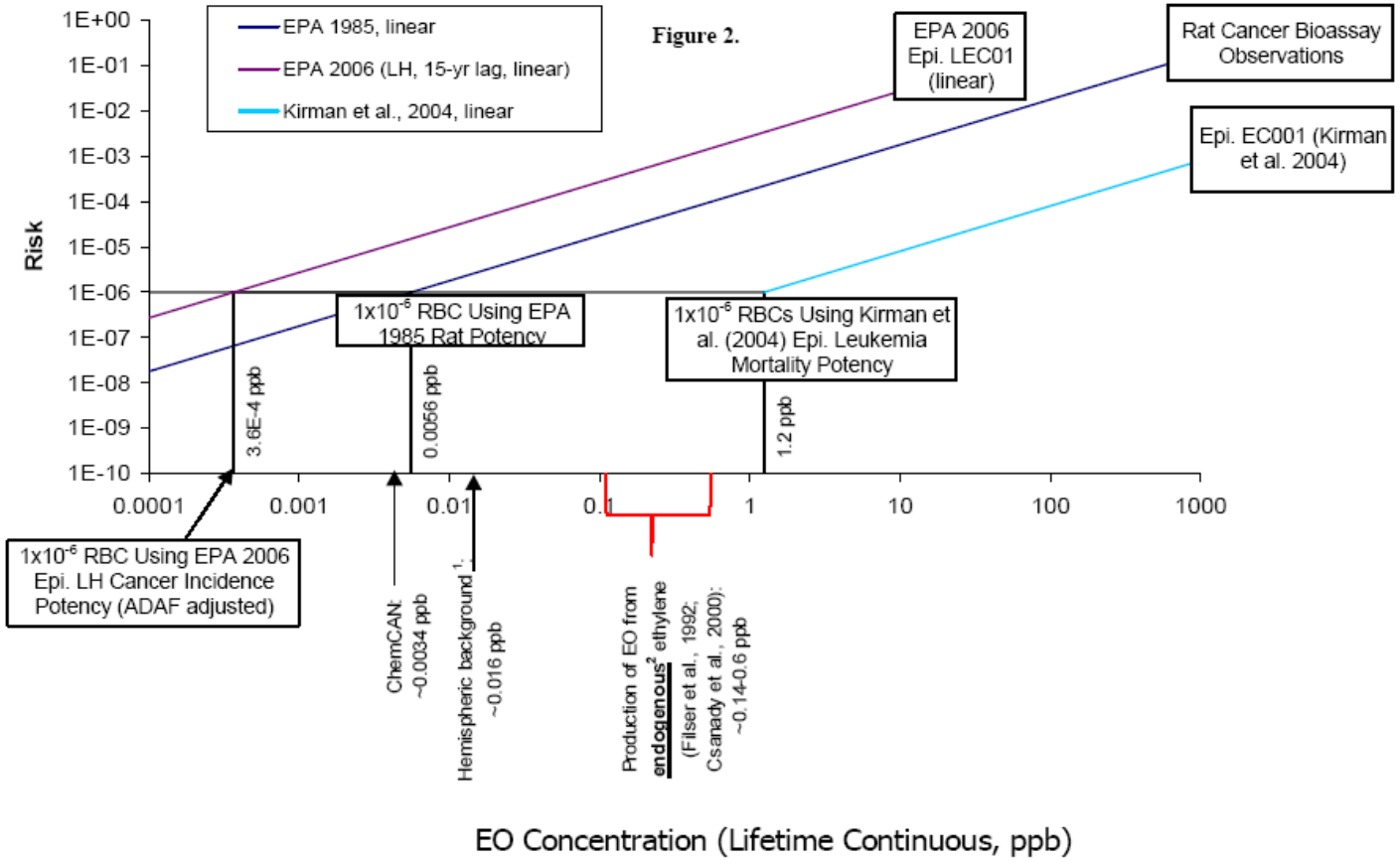
nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100E053.txt

- Major Changes Noted in 2011 Document- Unit Risk Estimate At or Below Level Proposed in 2006
- Final IRIS Assessment Not Yet Available

EO and Other IRIS Assessments

- Unit Risk Values in IRIS Update Likely in PPT Range!
- Not Biologically Plausible, Endogenous EO within our bodies is in the ppb range.
- Formaldehyde IRIS Assessment- Similar Situation
- EO is Not Considered a Strong Mutagen
- Continued Use of Conservative Modeling Approaches and Default Assumptions

EO Concentrations



1Natural EO produced by plants, microorganisms, water-logged soil.
2Endogenous ethylene normally produced from lipid peroxidation, oxidation of hemoglobin and methionine, and metabolism by intestinal bacteria

Revising the EO IRIS Assessment

- IRIS Update Needs WOE Approach
- IRIS Update Needs Detailed Characterization of MOA
- Realistic Characterization of Workplace Exposures Should be Included
- Exposures Should be Considered with Biological Plausible Background EO Levels To Calculate Reference Doses
- Use the Lessons from the Formaldehyde Assessment

EO Mode of Action

- From the EPA July 2011 Document:
  - Mutagenic Mode of Action
  - Epidemiology Data Selected Over Animal Studies
  - Early Life Exposure Adjustment Factor Added
  - Chronic Exposure Level Equating to 10^{-6} Lifetime Increased Cancer Risk is 0.0006 µg/m^3
  - Low Dose Extrapolation, Retrospective Exposure Assessments, and Exposure-Response Modeling of Epidemiological Data Contribute to Uncertainty

Who are We?

- **Bill Gulledge- Senior Director, Chemical Products & Technology, Manager, EO Panel**

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- **Sol Bobst, PhD, DABT- (former EO TRTG Chair, assisted in preparation).**
- **Bill Snellings- PhD (Toxdoc)**
- **EO TRTG and EO Panel Members**