

Comments to the Chemical Assessment
Advisory Committee for the IRIS Evaluation of
Ethylene Oxide:
Charge Question #4 Uncertainty

M. Jane Teta, Dr. PH, MPH

Exponent Inc.

On behalf of the American Chemistry Council

NIOSH Exposure Assessment Uncertainties Not Adequately Addressed

- No exposure data before 1975 and very little from 1976-1978
- Most worker exposures (approx. 70%) occurred during time of missing data (1943-1978); 86% hired before 1978;
- Validation testing of post 1978 data only
- Calendar year a major predictor of exposure post 1978 but regression model assumes no effect of calendar year prior to 1978
- NIOSH estimated concentrations decrease as go back in time from 1978;
Note: TLVs increase going back in time: 50 ppm early 1980s, 70s, 60s to 100 ppm in the 1950s and 40s

Both NIOSH and UCC exposure assessments suffer from absence of data prior to 1975 (NIOSH) and prior to 1957 (UCC).

Value of UCC Data To Increasing the Power of Study for Males Dismissed

- For Male “Lymphoid” Cancers:
 - NHL: UCC would add 12 more deaths to NIOSH 18
 - MM: UCC would add 3 more deaths to NIOSH 4
 - LL: UCC would add 2 more deaths to NIOSH 5
- Increases of 67%, 75%, and 40%, respectively, OR 60% overall to observed number of “lymphoid” cancers

Uncertainties for males would be less with both studies combined.

Breast Cancer Study: Potential Selection Bias Not Adequately Considered

- 2,437 (32%) women were not interviewed, mostly due to inability to locate
- Participation likely associated with exposure and with identification of breast cancers
 - Those interviewed were easier to locate and more likely to work longer (i.e., greater cumulative exposure) and be captured in cancer registry (higher rate of breast cancer) than those lost to follow up
 - Could explain elevated rates in highest exposure group
- Study found stronger relationship with duration of exposure than cumulative exposure

Inconsistencies in Breast Cancer Study Exposure-Response Trends Not Adequately Addressed

- Steenland (2003) noted difficulty in reaching causal interpretation due to these inconsistencies and interprets the data as “suggestive”
- Numerous failed attempts in IRIS modeling leading to two-piece linear spline model

Despite uncertainties in interview data and exposure-response trends and exposure assessment, Agency concludes “Confidence in the unit risk estimate is particularly high for the breast cancer component.”

Recommendations

- Revise IRIS assessment to incorporate UCC data
 - Uncertainties in NIOSH exposure assessment invalidate sole reliance on NIOSH Mortality study and exclusion of UCC study
 - Substantially increase study power for males
- Consider Dropping Breast Cancer as a target organ
 - Findings “suggestive” only and at highest exposures
 - Forced exposure-response model