

EPA Scientific Advisory Board Comments

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Exponent

Key Comments

- 1. Epidemiology evidence is not strong and does not suggest that EtO is a potent carcinogen**

Meta-SMR Trends through 1999 Publications: *Exposure Duration*

	Short	Medium	Long	P for Trend
Leukemia	1.04	1.46	1.71	0.27
NHL*		1.2	1.1	

*Non-Hodgkins Lymphoma

Meta-SMR Trends through 1999

Publications: *Latency*

	Short	Medium	Long	P for Trend
Leukemia	0.86	1.06	1.77 (0.97, 3.0)	0.11
NHL	1.86	0.89	1.16	0.32

SMRs of Studies through 2004 with the Longest Observation Time

	Teta	Olsen	Steenland (Females)	Coggon (Females)
All LH* N=103	0.59	1.29	1.00 (0.91)	1.32 (1.00)
Leukemia N=41	1.06	0.67	0.99 (1.02)	1.08 (0.55)
NHL N=40	0.99	0.91	1.00 (0.73)	1.46 (1.59)
Myeloma N=16	0	?	0.92 (1.19)	1.20 (0)

* Lymphohematopoietic

Key Comments

- 2. Underlying data should be used for dose-response, not publication summary statistics**

Underlying Data should be Used for Dose-response, not Publication Summary Statistics

- **Vital status and exposure estimates available from CDC for 17,530 study subjects not used**
- **EPA's model was based on summary odds ratios from publication**
 - Unable to examine other exposure cutpoints, responses, models (leukemia, multiple myeloma)
- **Results invalid**

Key Comments

- 3. Using incidence background rates with mortality study-based relative risks (RRs) creates biased results**

Invalid Use of LH Incidence Rates for Estimation of Excess Lifetime Risk

- EPA used RR estimates of LH mortality but applied background LH incidence rates to them over a lifetime
- Untested assumption that the exposure-RR trend from an incidence study would be the same
- EPA method introduces bias when agent is not related to all cell types equally as shown for leukemia (Teta et al. 2004)

Key Comments

4. Scientific evidence does not support adjustment for early life exposures

Scientific Evidence Does Not Support Adjustment for Early Life Exposures

- Children exposed to other alkylating agents are not at greater increased risk of leukemia or non-Hodgkin's lymphoma
- Children tolerated at least as high a dose of chemotherapeutic alkylating agents as adults
- Children have lower body burden of EO based on HEV adducts, relevant biomarker of EO exposure, in smoking studies