

Sept. 30 2014 EPA Ethylene Oxide SAB Teleconference

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Good afternoon. My name is Jane Teta, Principal Scientist at Exponent, a consulting company based in Menlo Park, CA. I continue to be a consultant to the American Chemistry Council. I have addressed IRIS review groups on several prior occasions and have authored numerous publications related to the potential health effects of ethylene oxide (ETO) over the past 25 yrs. The comments I am providing today are my own.

I am requesting that the EPA enhance their charge question related to uncertainty, that is, to “whether the qualitative discussions of uncertainty (Sections 4.1.4, 4.5, and 4.7 and Chapter 1) are clear, objective and scientifically appropriate”. Specifically, I recommend including discussion of whether the EPA has adequately covered the uncertainties of: 1) the NIOSH exposure assessment and 2) potential selection biases and inconsistencies in exposure-response trends in the NIOSH breast cancer incidence study.

The NIOSH exposure assessment is a key element in modeling the epidemiology data and in the ultimate unit risk estimates for both breast cancer and lymphoid tumors. The IRIS draft in the uncertainty section (4-47) discusses the NIOSH exposure assessment with a long list of positive attributes. The only uncertainty noted is the absence of exposure data during the extended follow up period, a rather unimportant issue. Several other more critical limitations are not mentioned, the most important of which is the absence of exposure data prior to 1976 and very little data from 1976-1978, when most of the worker exposures occurred. This is clearly noted by Dr. Steenland in Appendix H who says, “There is obviously more uncertainty about the estimation of exposures prior to 1975 when there was no sampling data. This uncertainty is of some concern in the sense that the majority of cumulative exposure metric for most workers is probably contributed by earlier, higher exposures.” The document fails to note that the validation procedure was limited to post 1978 data, that the effect of calendar year in the regression model was fixed at 1978 and as a result their estimates of maximum EO concentrations for years before 1978 implausibly decrease as you go back in

time. ACC's comments to the 2014 IRIS draft discussed these in greater detail, particularly as it relates to the absence of data prior to 1979. We request that the CAAC carefully examine EPA's treatment of the uncertainty issues regarding the NIOSH exposure assessment.

Another uncertainty issue relates to participation in the breast cancer interview in the Steenland et al. (2003) breast cancer incidence study. The IRIS risk assessment relies on the interview data from this study for calculation of a breast cancer unit risk estimate. One of the recognized uncertainties noted by the study authors is that 32% (2,437 women) were missing interviews, predominately due to inability to locate them. The potential for participation selection bias is noted in the uncertainty section of the IRIS document, but it is quickly dismissed concluding that non-participation in an interview would not be associated with breast cancer or ETO exposure. We disagree. The NIOSH authors of this study note the stronger relationship between duration of exposure than with cumulative exposure and concluded that a causal association with breast cancer is weakened by "possible biases due to non-response". Non-participants who could not be located would be expected to be shorter-term workers with less cumulative exposure and for whom breast cancer diagnoses could not be identified. Those with stable residence (and likely higher cumulative exposures) are more likely to be interviewed and their breast cancer diagnoses identified. The NIOSH authors interpret the data as *suggestive* for those with higher cumulative exposures to ETO. They also note their difficulty in reaching a causal interpretation due to inconsistencies in the exposure-response trends. This is reflected in the numerous attempts to model these data for unit risk estimation leading ultimately to the selection of a two-piece linear spline model. The uncertainties associated with the breast cancer incidence study are worthy of greater consideration in the context of the IRIS document statement (4-76), "Confidence in the unit risk estimate is particularly high for the breast cancer component."

My thanks to the Agency and the CAAC for this opportunity to offer my comments. By strongly urging EPA to revise its risk assessment to incorporate these and other considerations, the CAAC will contribute to a much more scientifically credible assessment of ethylene oxide exposures.