Review of EPA's Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide

ATSDR supports the EPA classification of ethylene oxide as "carcinogenic to humans" (as well as the NTP classification of "known to be a human carcinogen) based upon several routes of evidence (an overall weight of evidence) not limited to only human epidemiological data for the inhalation route of exposure. The reason for needing a weight-of-evidence approach is the rather weak relative risks found in the epidemiology studies. EPA has taken a similar approach in their conclusions using epidemiological data, animal data, and mutagenic/genotoxic data.

ATSDR has found that while the IRIS document is clear as to the approach taken for carcinogenic classification it does not discuss the short falls of the Steenland analysis of the NIOSH data and other epidemiology studies. There are many confounders in these studies and there are design limitations that may increase or decrease the measured responses. Presentation of uncertainty and limitations in section 3 is warranted. It is noted that epidemiologic data suggests lymphohematopoietic cancers are more substantiated than breast cancers but little discussion states why this conclusion is reached. Is this simply based upon the relative risk values or odds ratios? The study by Adam is not mentioned until page 227 but could be used to build the case for a breast cancer link.

ATSDR finds the NIOSH study (as analyzed by Steenland) the most appropriate to use based on the cohort size, the completeness of the study, and good exposure assessment. EPA's presentation of the weight-of-evidence is well done and builds a case that concludes that ethylene oxide is a human carcinogen with which ATSDR concurs. ATSDR suggests adding more discussion to the uncertainties and limitations of the epidemiological studies in section 3 and identifying any ongoing studies that may help fill data limitations of the current assessment.

Adam A, Bardo H, Adany R (2005). Increased genotoxic susceptibility of breast epithelial cells to ethylene oxide. Mutation Res, 585:120-126