

## **An evaluation of reported no-effect chrysotile asbestos exposures for lung cancer and mesothelioma.**

Pierce, J.S., McKinley, M.A., Paustenbach, D.J., Finley, B.L.

Numerous investigators have suggested that there is likely to be a cumulative chrysotile exposure below which there is negligible risk of asbestos-related diseases. However, to date, little research has been conducted to identify an actual “no-effect” exposure level for chrysotile-related lung cancer and mesothelioma. The purpose of this analysis is to summarize and present all of the cumulative exposure-response data reported for predominantly chrysotile-exposed cohorts in the published literature. Criteria for consideration in this analysis included stratification of relative risk or mortality ratio estimates by cumulative chrysotile exposure. Over 350 studies were initially evaluated and subsequently excluded from the analysis due primarily to lack of cumulative exposure information, lack of information on fiber type, and/or evidence of significant exposures to amphiboles. Fourteen studies meeting the inclusion criteria were found where lung cancer risk was stratified by cumulative chrysotile exposure; four such studies were found for mesothelioma. All of the studies involved cohorts exposed to high levels of chrysotile in mining or manufacturing settings. The preponderance of the cumulative “no-effects” exposure levels for lung cancer and mesothelioma fall in a range of approximately 25–1000 fibers per cubic centimeter per year (f/cc-yr) and 15–500 f/cc-yr, respectively, and a majority of the studies did not report an increased risk at the highest estimated exposure. Sources of uncertainty in these values include errors in the cumulative exposure estimates, conversion of dust counts to fiber data, and use of national age-adjusted mortality rates. Numerous potential biases also exist. For example, smoking was rarely controlled for and amphibole exposure did in fact occur in a majority of the studies, which would bias many of the reported “no-effect” exposure levels towards lower values. However, many of the studies likely lack sufficient power (e.g., due to small cohort size) to assess whether there could have been a significant increase in risk at the reported noobserved- adverse-effects level (NOAEL); additional statistical analyses are required to address this source of bias and the attendant influence on these values. The chrysotile NOAELs appear to be consistent with exposure-response information for certain cohorts with well-established industrial hygiene and epidemiology data. Specifically, the range of chrysotile NOAELs were found to be consistently higher than upper-bound cumulative chrysotile exposure estimates that have been published for pre-1980s automobile mechanics (e.g., 95th percentile of 2.0 f/ cc-yr), an occupation that historically worked with chrysotile-containing friction products yet has been shown to have no increased risk of asbestos-related diseases. While the debate regarding chrysotile as a risk factor for mesothelioma will likely continue for some time, future research into nonlinear, threshold cancer risk models for chrysotile-related respiratory diseases appears to be warranted.

Keywords Asbestos, chrysotile, mechanics, threshold