

**Agency for Toxic Substances and Disease Registry (ATSDR) Comments on the Interagency
Science Discussion Draft IRIS assessment of Libby Amphibole Asbestos (dated August 2014)**

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**EPA TOXICOLOGICAL REVIEW OF LIBBY AMPHIBOLE ASBESTOS
COMMENTS FROM THE AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY**

I have reviewed the most recent version of *TOXICOLOGICAL REVIEW OF LIBBY AMPHIBOLE ASBESTOS. In Support of Summary Information on the Integrated Risk Information System (IRIS)*. Because ATSDR has commented previously I focused on the areas that have changed since we last saw it. These areas are outlined on EPA's website and include:

- Added a section on fiber determinants of toxicity
- Added a formal mode-of-action analysis for carcinogenicity
- Added graphical display of the fit to data for the main cancer and noncancer models as well as for a broader range of models
- Added a more detailed review of the literature on localized pleural thickening to further support the appropriateness of that health endpoint for deriving the RfC
- Added support for the EPA's choices of statistical models, metrics and BMRs for the exposure-response analysis
- Added analyses of pleural abnormalities using recently published studies on two other Libby Amphibole asbestos-exposed cohorts to the extent data permit
- Re-evaluated uncertainty factors

The re-writes and clarifications were helpful and supportive of the document; as were the new graphics. Both added to the clarity and readability of the document. No additional

suggestions for clarifying the document are being made. There are however two areas for which I have comments.

- 1) Table 3-2 Determinants of Fiber Toxicity. Fiber length has been assigned a “++” for carcinogenicity (suggested role but data not conclusive). The evidence that longer fibers are more carcinogenic is stronger than the table suggests. When the database taken as a whole is examined the work of Stanton, Berman, Davis and Jones, Lippman, Case, and others point to long fibers as being the most toxic of fibers. Combine these findings with proposed mechanistic methods of long fiber toxicity (frustrated macrophages, lodging in airways, decreased clearance, etc.) and the literature suggests a rating of +++ (suggested role with substantial data support). The current argument in the literature is more about the role and toxicity of short fibers; the role of long fibers is established.
- 2) The uncertainty factor for subchronic to chronic extrapolation. The justification for using an uncertainty factor of 10 (as opposed to 1 or 3) is that, “Using the model selected for derivation of the RfC, the probability of LPT increases 10-fold between 28-years TSFE (the median in the population of workers used for analysis) and 70-years TSFE.” It does not seem appropriate to justify a subchronic to lifetime exposure uncertainty factor by modeling a lifetime exposure from the subchronic data and noting that the difference is the same magnitude as the UF. To do so does simply models the predicted response and says nothing about the uncertainty of the extrapolation. Why not model the lifetime risk (from the 28-year data) and then apply the uncertainty factor to that value? Similar to BMD modeling substituting for a LOAEL to NOAEL extrapolation and uncertainty factor, the subchronic to chronic modeling could substitute for the subchronic to chronic extrapolation and associated uncertainty factor (or a modified UF factor could be used, e.g. 3).

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