

Dr. Carrie Redlich's Preliminary Comments

Section 4.5 Synthesis of Non-Cancer Effects

1. Is the Toxicological Review logical, clear, and concise? Has EPA clearly, and in sufficient detail, presented and synthesized the scientific evidence for health hazards from Libby Amphibole asbestos?

Overall, Yes. It could be more concise and a few points could use clarification.

1) Given the extensive literature on non-Libby asbestos forms of asbestos, in summarizing the non-cancer health outcomes and possible mechanisms it would be helpful to state more clearly whether any of the findings / studies suggest any major differences between Libby Amphibole and other forms of asbestos as far as the types of health effects and modes of action. Do we have reason to suspect that Libby asbestos pathophysiologically or mechanistically differs from other asbestos? While there likely are differences in the degree of toxicity, do Libby plaques differ from other asbestos-induced plaques? Are the cellular and molecular changes seen in response to Libby asbestos (e.g. cytotoxicity, increased ROS) substantively different than what has been reported with other types of amphibole asbestos?

If the answer is no, then it would be helpful to:

a) Frame the summary discussion with that in mind, and also shorten some sections. Is the bottom line, *"there is currently insufficient evidence to establish the non-cancer mode of action of Libby asbestos"* vs. studies so far on Libby asbestos suggest same modes of action as other asbestos"

b) Shorten some sections describing 'standard' clinical asbestos-related findings, and avoid general statements that may have inaccuracies. For example (4-72) *"The scarring of the parenchyma tissue of the lung contributes to measured changes in pulmonary function, including..... restrictive pulmonary deficits from impacting the elasticity of the lung"*. (omit *"from impacting the elasticity of the lung"*).

2) The potential impact of smoking on other nonmalignant respiratory diseases (and lung cancer) is of sufficient importance (and controversy) that it should be mentioned in the summary. Other nonmalignant respiratory diseases include COPD, upper respiratory tract diseases, asthma, and other diseases, COPD being the most important of these. The statement *"These diseases are consistent with asbestos toxicity"* does not clarify what diseases "these" refers to and is overly broad. (page 4-73)

(Very minor wording edits:

- 1) Clarify units or % when referring of FEV1 or FVC, usually % predicted. (e.g. 4-72)
- 2) page 4-72 line 3 – some typo – sentence as written unclear.
- 3) LPT and DPT are used in Section 4.5 but not defined until later.
- 4) 4-72 'fibrotic damage' – fibrosis or fibrotic changes)

2. Please identify any additional peer-reviewed studies from the primary literature that should be considered in the assessment of noncancer and cancer health

effects of Libby Amphibole asbestos.

The literature review is quite thorough.

Two very recent articles related to non-occupational exposure in Minneapolis, Minnesota should be included, given the concerns regarding non-occupational sources of Libby asbestos and risks of exposure.

- 1) Alexander et al. EHP 2012. Radiographic evidence of nonoccupational asbestos exposure from processing Libby vermiculite
- 2) Adgate et al. Modeling community asbestos exposure... J Exposure Sc and Envir Epi 2011.
- 3) It (obviously) would be helpful to include Dr. Lockey's submitted publications, if possible.

Section 4.7 Susceptible Populations

1. Is the Toxicological Review logical, clear, and concise? Has EPA clearly, and in sufficient detail, presented and synthesized the scientific evidence for health hazards from Libby Amphibole asbestos?

This section cites a wide range of animal and human studies that may provide information regarding the health effects of asbestos in susceptible populations (e.g. age, gender, race).

Since so many of the studies are based on white male occupational cohorts (and the need for sufficient latency), the data regarding susceptible populations and any type of asbestos, let alone Libby asbestos, is limited. This section could be better organized and more succinctly summarized.

2. Please identify any additional peer-reviewed studies from the primary literature that should be considered in the assessment of noncancer and cancer health effects of Libby Amphibole asbestos.

None aware of related to susceptibility.

Section 5.4 Cancer Exposure Assessment

Selection of Principal Study; and Endpoint Selection

Questions II.B3 and II.B4

3. An occupational cohort of workers from Libby, MT exposed to Libby Amphibole asbestos (i.e., the Libby worker cohort) was selected as the basis for the derivation of the inhalation unit risk (IUR). Please comment on whether the selection of this study population is scientifically supported and clearly described. If a different study population is recommended as the basis for the IUR, please identify this study and provide scientific support for this choice.

Yes. The Libby worker cohort is scientifically supported to use for cancer endpoints. Any cohort has limitations, but this cohort appears to be the best available cohort for cancer endpoints. Limitations of this cohort include limited smoking information. Also outcomes are based on death certificates, which could undercount cancer endpoints, especially mesothelioma. The EPA analysis attempts to take into account these factors.

4. Mortality from lung tumors and mesothelioma in the Libby worker cohort was selected to serve as the basis for the derivation of the IUR. Please comment on whether this selection is scientifically supported and clearly described. If a different health endpoint is recommended for deriving the IUR, please identify this endpoint and provide scientific support for this choice.

The use of lung cancer and mesothelioma in the Libby cohort is scientifically supported and clearly described. Issues with using death certificates are addressed.

Miscellaneous General Comments

I may have missed the following, given the length of the document, but it would be helpful to have a clear comparison of the Libby asbestos findings with other asbestos risk assessments / reviews, including a Summary / Comparison Table. The adverse health effects of asbestos have been well studied. The key question is how this risk assessment of Libby asbestos compares to other asbestos reviews / risk assessments – the studies, exposures, methods, results.

Extensive background is given about asbestos types, Libby asbestos, etc. Additionally a Summary Table or Figure describing the major cohorts (Libby workers, community, Marysville plant), and the studies / exposure info associated with each would be helpful.