

Statement for Public Teleconference for the SAB review of “Draft Toxicological Review of Libby Amphibole Asbestos” (EPA/635/r/002a)

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Prior comments

1. Public Comments from Elizabeth Anderson, Exponent, Inc. (01/27/2012)
 - Issues identified in previous IRIS assessments
 - Specific comments on draft toxicological review for LAA
 - Practical and societal implications of proposed RfC
2. Public Comments from Elizabeth Anderson, Exponent, Inc. - Addendum (02/07/12)
 - Relationship between RfC and cancer risk
 - Effect of RfC on data quality requirements and costs
3. Additional Comments from Elizabeth Anderson and David Hoel, Exponent, Inc., (04/09/2012)
 - Selection of critical endpoint
 - Derivation of draft RfC
 - Practical considerations

Critical Endpoint Selection

“The SAB agrees that the selection of radiographic evidence of localized pleural thickening (LPT) in humans is the appropriate critical effect for the derivation of the RfC. LPT is a structural, pathological alteration of the pleura, and is associated with reduced lung function. The presence of LPT itself is a risk factor for other asbestos-related diseases, including asbestosis, mesothelioma and lung cancer, a point that EPA should also include. The SAB identified additional evidence and a more detailed review of the literature is needed to further support this view.” *[SAB Draft Letter, April 11, 2012 (SAB 2012) p. 10]*

Critical Endpoint Selection

- LPT is a marker of exposure; any association with other endpoints that occur because of asbestos exposure is not clearly supported by the data.
- Other non-cancer endpoints are biologically distinct from LPT and should be separately derived. Other non-cancer endpoints do occur with increasing cumulative exposures as a progression from LPT and should be treated independently as critical endpoints but should not be combined for dose response evaluation.
- LPT appears to occur at very low levels of exposure but current data do not clearly show that LPT is associated with adverse effects or that they are on a biological pathway to other adverse effect. If other non-cancer endpoints are considered, separate dose response curves and RfCs should be derived.
- ILO (2000) definition of LPT places LPT on the parietal part of chest wall not on the visceral pleura therefore they are unlikely to be involved in the biological progression to other end points noted in the above statement and not with lung function deficit.

Critical Endpoint Selection

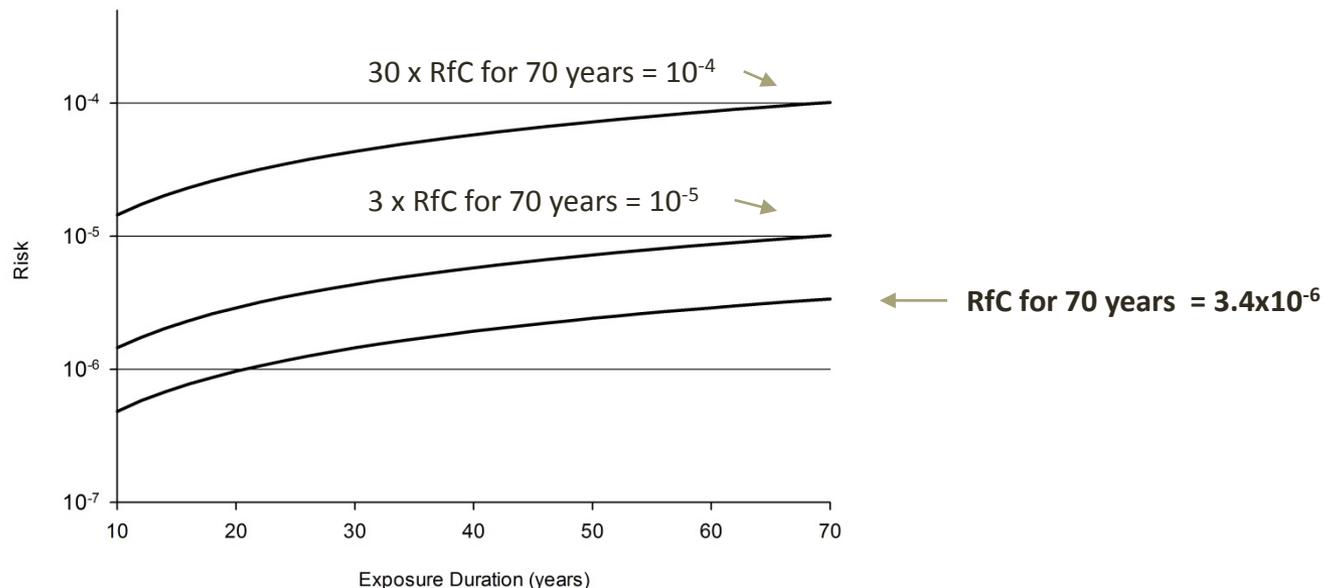
- No data set seems reliable for deriving an RfC based on LPT. However, if the Rohs et al cohort is to be used, the entire cohort should be evaluated and with the pulmonary function data which is expected to be completed later this year.
- Biomarkers of exposure have not typically been the choice for deriving RfCs and RfDs.
- The NAS 2006 report addressed the importance of chemical biomarkers and concluded that our ability to measure the presence of markers exceeds our ability to evaluate related risk.
- Using biomarkers for derivation of risk based regulatory levels could lead to highly precautionary values that approach zero tolerance; a policy abandoned in the early 70s as unachievable.

Derivation of the RfC

- Use of the proposed RfC including the division by 60 years (or 70 years as proposed by the SAB) leads to false positives;
- The RfC will be below the point of departure adjusted down by uncertainty factors (UFs) for almost all exposure scenarios used in risk assessment producing a Hazard Quotient above 1 when the actual exposures are below the level of concern, i.e., the UF-adjusted POD.
- The proposed POD is currently 6000 times lower than the POD. EPA normally places a 3000 cap on cumulative uncertainty with the notation that uncertainties exceeding this level make the resulting guidance too uncertain for use.
- Possibly reduce the uncertainty/safety factor of 10 for database deficiencies to 3 when other asbestos literature is included.

Derivation of the RfC

- The proposed RfC value of 0.00002 f/ml will drive the risks in all circumstances at the level of 10^{-6} not 10^{-5} as stated in the current SAB 2012 draft letter/report 2012.



- Because of the profound implications of this draft RfC, be very certain that it is well founded on sound science .