Comments to full SAB Panel on "Draft Toxicological Review of Libby Amphibole Asbestos" (EPA/635/r/002a)

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I have previously provided detailed written and oral comments to the SAB Libby Amphibole Asbestos Review Panel (Panel). In those earlier comments I have pointed out profound implications of the draft toxicological review in particular related to the derivation of a reference concentration level (RfC) for health effects other than cancer, the first of its kind for any form of asbestos. This shorter document outlines the important points that I have made related to the proposed toxicological assessment for effects other than cancer (non-cancer effects). Also of importance is the fact that these issues are embodied in the charge questions to the Panel.

Although members of SAB Panel have made certain statements that acknowledge their understanding of these comments, the Panel as a whole in its draft report to EPA has not sufficiently dealt with the scientific, practical and, policy implications that have been raised my me and other commenters. Consequently, the SAB Committee should return this matter to the Panel for reconsideration so that EPA can benefit from more comprehensive guidance in response to the charge questions.

Non-Cancer Risk Will Drive Future Asbestos Risk Assessment Currently Based on Cancer

In my earlier comments, I demonstrated that the proposed RfC, in most cases, would likely drive any risk assessment. An unacceptable non-cancer hazard would be reached well before the upper bound of the acceptable cancer risk range for decision making, a risk of one in ten thousand, and lie close to and even below the lower bound of one in one million. Accordingly the draft RfC, if adopted, will drive the risk up to 100 fold lower than the level dictated by the public health protection for long established cancer endpoints of mesothelioma and lung cancer.

Background Levels of Asbestos in Air

The proposed RfC of 0.00002 f/cc is so low that it is in within background. The use of this level will frustrate cleanup efforts and confuse the public.

Background levels of asbestos vary depending on location but the current estimate is on the order of 0.00001 f/cc for rural areas and up an order of magnitude higher, i.e., 0.0001 f/cc, in urban areas (ATSDR 2001). Distinguishing the incremental contribution of source contamination over background will be difficult, time consuming, and costly.

Measurement Sensitivity

Upon adoption of the extremely low air concentration that is proposed for the RfC, large amounts of current and historical sampling data from Libby, MT would be of limited utility. For example, the current detection limit for Libby ambient air sampling is about twice as high as the proposed RfC meaning that these data cannot discern if a hazard exists when compared to the proposed RfC. At Libby, asbestos fibers are typically not detected but on occasion fibers are found. Although the levels are low, when compared to the proposed RfC they would indicate a hazard exceeding a hazard quotient of 1 which under Superfund policies would warrant action. Similarly, current and past air data from other sites and locations will need to be reevaluated to determine if the public is protected to this much lower standard. In all likelihood, new sampling data will be required to reach the sensitivities for these evaluations and to try to distinguish any fibers found from background contributions.

Application to other forms of asbestos

While most background asbestos in air in the US has been identified as chrysotile asbestos, there are areas where amphibole asbestos varieties, including Libby Amphibole, tremolite and other forms, have been found from naturally occurring background sources. While the EPA draft assessment is focused on Libby Amphibole Asbestos (LAA) there is no convincing literature on the association of asbestos exposure and the occurrence of localized pleural thickenings (LPT) that would preclude application of these results to all types of asbestos exposures. Since this RfC is the first for any type of asbestos it is likely to be used to define non-cancer potency information for all other forms or asbestos.

The Draft RfC is Derived in an Atypical Manner: Adjusting Point of Departure by 60 Years.

No other RfC in the IRIS data base has be pre-adjusted for a lifetime of exposure by dividing by 60 or as the Panel is proposing by 70 years for lifetime exposure making the misunderstanding and misused of this RfC enviable. All other RfCs in the IRIS data base, so far as I know, are also expressed in concentration terms but these other RfCs have not had, in addition to safety factors (which in the draft document are 100), been further adjusted by division of a lifetime of exposure. For non-cancer endpoints, this accounting takes place during an actual risk assessment process where the RfC is compared to the average daily concentration calculated by dividing the cumulative exposure by the actual years of exposure that have occurred in the particular instance being assessed to arrive at the average daily concentration. If this average daily concentration divided by the RfC exceeds a Hazard Index of one, risk management action is mandatory.

The problem in this instance arises because asbestos exposures are evaluated in a different way from exposures to other toxic substances. First, the concentration metric is fibers per volume of air, rather than the mass-based concentration used for other toxic substances. Second, the use of cumulative exposure (f/cc-years) as the point of departure (POD) for health effects is also uncommon; typically, the POD is expressed in terms of concentration or dose.

A reference concentration (RfC) is an air concentration that is deemed safe over a lifetime exposure. Typically these are derived from lowest effects or no effects levels determined in animal or less often from human epidemiologic studies. Uncertainty factors are applied to the effects levels to ensure the RfC is sufficiently protective of the public. In this case, EPA has estimated a POD for health effects in terms of a cumulative exposure (f/cc-years) further reduced by application of uncertainty factors (100 fold reduction). To effect the conversion from cumulative to concentration (to cancel the units of "years" from the POD) EPA has divided the POD by an additional factor of 60 years to represent a lifetime exposure less a 10 year lag time. However, this conversion will overestimate non-cancer risk (hazard quotient) when applied in risk assessment and, in some cases, will result in false positives prompting action where none is warranted. This is because the exposure concentration that is compared to the RfC to generate the hazard quotient is by convention and practice the average concentration for the years over which exposure occurs, not the concentration averaged over a person's lifetime. In practice, it is rare that an individual is exposed over an entire lifetime.

Although consistent with the definition of an RfC, *"[a]n estimate (with uncertainty spanning perhaps an order of magnitude) of a continuous inhalation exposure for a chronic duration (up to a lifetime) to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime*", the application of the lifetime adjustment factor presents a quandary for asbestos risk assessors because, for any situation involving less than lifetime exposure, the ratio of the specific exposure to RfC (the hazard quotient) will exceed the ratio of the cumulative exposure to the POD. For example, the EPA standard assumption of residential exposure duration is 30-years and for an individual exposed at a level just over the RfC for this period would have a hazard just over 1 which would be potentially unacceptable. However the same exposure would only result a cumulative exposure just over one-half of the uncertainty factor-adjusted POD; this would indicate a unacceptable hazard where none exists; a false positive. In fact, typical environmental exposures occur for less than a full life time, e.g. a childhood exposure of 6 years, average residential exposure of 9 years or at the 95%ile, 30 years.

The solution to this problem is simple, leave the reference level in its original units of cumulative exposure, i.e., f/cc-years, made equivalent to the POD/UF. This should present no problem to a risk assessor as the conversion from an air concentration exposure to a cumulative exposure is a trivial matter requiring only knowledge of the number of years over which the exposure occurs which is a prerequisite for any risk assessment. Alternatively the POD could be established by modeling based on concentration, a topic not addressed in my comments.

<u>Endpoint Selection: Whether Pleural Plaques are an Appropriate RfC Endpoint</u>

To the extent that LPT is not an adverse effect in itself or a precursor to a critical effect (e.g., impaired lung function) its selection is inconsistent with the basic definition of the critical effect provided in EPA's IRIS Glossary: "Critical Effect: The first adverse effect, or its known precursor, that occurs to the most sensitive species as the dose rate of an agent increases." While there is every reason to think that at some levels of exposure LPT is correlated with pulmonary function deficits, the word 'associated' with as

expressed in the Draft Document has less certain scientific meaning. Further the evidence that LPT causes pulmonary function deficits has been seriously challenged by other comments received by the Panel (Mohr, DeSesso). In addition, I find that many of the statements made by the SAB members are consistent with my comments and those of Drs. Mohr and DeSesso on the issue of whether localized pleural thickenings (LPT) should be the appropriate critical endpoint for the RfC derivation

For this draft assessment, we are in the rare position of deriving the inhalation reference concentration (RfC) from human data rather than from laboratory animal studies. This fact should remove some of the precautionary measures that are often involved when selecting the critical endpoint from experimental studies. If the quantitative relationship between LPT (pleural plaques) is not clearly confirmed to be associated with an adverse effect such as decreased lung function, and the biological mechanism for such a relationship is unknown, then LPT (pleural plaques) can be viewed only as a marker of exposure that is not verifiably causative of an adverse effect or on a biological pathway to cause disease.

Markers of exposures from human data have not typically formed the bases for RfC derivation. Further setting this precedent will present challenges for many other substances in the environment where biomonitoring data define markers of exposure for many substances. Setting RfCs based on these markers will be highly precautionary and will raise serious challenges of social and economic consequence, reminiscent of the early 1970s when zero risk tolerance was abandoned in favor of risk assessment and risk management policies (Albert et al 1977).

The recommendations made by the NAS to EPA in Chapter 7 of the formaldehyde review (NRC 2011) under the banner, "Reframing the Development of the IRIS Assessment" were described by NAS as "critical for the development of a scientifically sound IRIS assessment" (NRC 2011, p 121). Of particular importance are the recommendations that pertain to "Selection of Studies for Derivation of Reference Values and Unit Risks" which include recommendations to establish clear guidelines for study selection, balance strengths and weaknesses, evaluate human vs. experiment evidence, consider combining estimates among studies and "Calculation of Reference Values and Unit Risks" which includes recommendations to justify assumptions, carefully consider and explain models used, justify statistical and biological models, and describe the fit to the data, determine points of departure, assess analyses that underlie the points of departure, provide the range of estimates and describe the effect of uncertainty factors on the estimates and assess the adequacy of documentation to support conclusions and estimates. Further emphasizing the importance of these recommendations, the Chairman of the formaldehyde committee, Dr. Jonathan Samet, echoed these themes in his testimony before Congress: "The committee's review of the EPA's draft IRIS assessment of formaldehyde identified both specific and general problems with the document. The persistence of the problems encountered with the IRIS assessment methods and reports concerned the committee, particularly in light of the continued evolution of risk-assessment methods and the growing societal and legislative needs to evaluate many more chemicals in an expedient manner."

Many of these themes also are expressed by individual states and federal agencies in their reviews of these EPA draft health assessment documents, including the subject draft toxicological assessment for

Libby Amphibole under current review (U.S. EPA 2011b). The agencies that have provided comments on the Draft Libby Amphibole review include the National Center for Environmental Health (NCEH)/Agency for Toxic Substances and Disease Registry (ATSDR), Centers for Disease Control and Prevention (CDC), Department of Defense (DOD), National Institute of Environmental Health Sciences (NIEHS), National Institute for Occupational Safety and Health (NIOSH), and Office of Management and Budget (OMB).

Further, the U.S. Government Accountability Office's report on chemical assessments also makes it clear that EPA faces both long-standing and new challenges in implementing the IRIS Program (GAO 2011). The GAO report also reiterates issues raised previously by NAS concerning clarity and transparency, and the other general recommendations by the NAS (summarized above). Therefore, we are seeing a broad consensus emerge that it is a high priority to improve the scientific integrity of risk assessments. This is the context and challenge for this SAB as it considers the Draft Toxicological Review of Libby Amphibole Asbestos. The EPA faces a substantial challenge to improve the process and the underlying science that supports the assessments that are entered into the IRIS data base. This draft report should be reconsidered by the Panel in light of the comments that I and others have raised concerning serious scientific and public health policy issues that require reevaluation before the EPA can finalized this risk assessment document for Libby Amphibole Asbestos.