

**Comments to EPA Science Advisory Board
Asbestos Committee**

On

**Office of Solid Waste and Emergency Response (OSWER)
Proposed Approach for Estimation of Bin-Specific Cancer
Potency Factors for Inhalation Exposure to Asbestos**

Submitted July 7, 2008 by

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On behalf of 83 co-signers (see attached list)

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Factors for Inhalation Exposure to Asbestos**

The Proposed Approach¹ is fundamentally flawed and cannot be perfected. It suffers from the following defects:

- EPA's Cancer Risk Assessment Guidelines require that OSWER complete a weight of evidence narrative before attempting dose-response assessment. Here, OSWER is doing the opposite. Its approach prejudices the hazard evaluation and toxicity assessment that remain to be done. Its approach is inconsistent with EPA's established policy on asbestos risk.
- The proposed OSWER method will produce unreliable estimates of risk and should not be used for public health purposes. It relies on exposure assessments that are irreparably flawed, a problem that cannot be overcome by statistical modeling.
- The proposed OSWER method excludes and ignores critically important data. Large numbers of mesothelioma deaths from highly relevant and well-conducted studies will not be considered.
- There have been no significant new studies or data since 2003 that provide a compelling basis for another risk assessment proposal.
- The new proposal has not addressed all of the recommendations made by the panel that reviewed the 2003 proposal.

¹ Brattin W. Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos. EPA Office of Solid Waste and Emergency Response, April 23, 2008.

- OSWER has not validated the model and methods it intends to use. It has not conducted sensitivity analyses and goodness of fit testing.
- Sensitivity analysis done in 2003 shows that the entire modeling exercise is too unstable to use.
- The difference in lung cancer risk experienced by Quebec miners and South Carolina textile workers has not been adequately explained, but will have significant impacts on the results generated by the proposed method.
- There is no compelling scientific basis for estimating different potency factors for lung cancer by fiber type.

Background

EPA's current risk assessment methodology for asbestos and cancer has been in place since 1986 when the agency assumed that chrysotile and amphiboles were equally potent for causing both lung cancer and mesothelioma.² In 1989, when adopting a ban on asbestos products, EPA again concluded that its risk assessment should assume that all asbestos fibers have equal potency.³ OSHA reached the same conclusion in 1986 and 1994.

However, since the late 1990s, OSWER has been developing potency factors for use in risk assessment based on the assumption that different asbestos fibers have different potencies. With each new draft consultant report, the estimated potency of chrysotile relative to the amphiboles has decreased. And, at every step the suggestion that chrysotile might not cause mesothelioma at all has been stronger.

In the late 1990s EPA hired Drs. Wayne Berman and Kenneth Crump to work on an assessment method that distinguished risks for different fibers types and dimensions. Berman/Crump's 2001 draft report estimated that chrysotile is only 20% as potent as amphiboles for lung cancer, leaving open the possibility that chrysotile and the

² 51 Fed. Reg. 22612 (1986).

³ 54 Fed. Reg. 29467. (1989)

amphiboles are equally potent.⁴ The estimate for mesothelioma was that chrysotile was only 0.2% as potent as amphiboles.

The Berman/Crump proposal was reviewed by an EPA expert panel, but not the SAB, in 2003. Based in part on these expert comments,⁵ Berman/Crump submitted a revised 2003 report that increased the relative chrysotile potency for lung cancer to 26% of the amphibole potency, again leaving open the possibility of equal potency.⁶ However, the chrysotile potency for mesothelioma was reduced to only 0.13% of the amphibole potency, with the added suggestion that chrysotile might not cause mesothelioma at all.⁷

The new 2008 Proposed Approach (OSWER/Brattin/Crump) is similar to the Berman/Crump analyses, but differs from them in several important ways. First, it uses more complex mathematical and statistical modeling tools. Second, it applies the mathematical models to more subgroups of asbestos (or “bins” defined by fiber type, length and width). Third, it converts historic exposure data, typically measured by total dust counts or fiber counts, into new fiber type and dimension values as if the old samples had been analyzed with the newer transmission electron microscope (TEM) techniques. Fourth, it excludes from its analysis several important published studies as well as many individual mesothelioma cases.

The 2008 OSWER/Brattin/Crump Approach is inconsistent with EPA’s cancer risk assessment guidelines.

⁴ Eastern Research Group. Report on the Peer Consultation Workshop to Discuss a Proposed Protocol to Assess Asbestos-Related Risk. May 30, 2003. Pp 2-2, 2-3.

⁵ Eastern Research Group 2003

⁶ Berman DW and Crump KS. Technical support document for a protocol to assess asbestos-related risk. EPA #9345.4-06, October 2003. P 1.4

⁷ Berman and Crump 2003 p 1.4 “the possibility that pure chrysotile is non-potent for causing mesothelioma cannot be ruled out by the epidemiology data.” And p 7.49. “the data are consistent with the hypothesis that all of the mesotheliomas occurring in cohorts exposed primarily to chrysotile are due to small amounts of amphibole contamination within the chrysotile”

EPA's cancer risk assessment guidelines require that a weight of evidence analysis precede development of a dose-response assessment. OSWER is aware that EPA is undertaking a full asbestos toxicity assessment for its Integrated Risk Information System (IRIS) that will go beyond the epidemiological modeling and will "integrate important data from other sources, including animal exposure-response data, lung burden data, *in vitro* data, mode of action data, non-cancer effects data, and differential life-stage sensitivity data."⁸

EPA concluded in 1989 "definitive conclusions concerning the relative potency of various fiber types in inducing mesothelioma cannot be made on the basis of epidemiological information."⁹ EPA has not changed this policy determination. OSWER, however, intends to do exactly what EPA has rejected; stating that the proposed approach "is focused only on the fitting of epidemiological exposure-response data to cancer risk models, and does not seek to integrate important data from other sources."¹⁰

This is not an abstract, academic exercise. OSWER plans "to apply these cancer potency factors in risk assessments for Superfund sites" immediately after the SAB review is completed even though it recognizes that "all of these other data sources provide valuable information on asbestos toxicity and carcinogenicity." OSWER should wait rather than act on an admittedly "intermediate step" as if it were the final agency determination about community risk.

The 2008 OSWER/Brattin/Crump method will produce results that can't be trusted. There are insurmountable problems with uncertainty and unreliability

Elegant mathematics does not ensure good public policy, especially when the math is applied to substantially incomplete and unreliable data. The risk assessment model being proposed is constructed around probabilities and possibilities. It will produce specific

⁸ Brattin 2008 p ES-2

⁹ 54 Fed. Reg. 29470 (1989).

¹⁰ Brattin p ES-2

estimates of risk surrounded by fuzzy zones of uncertainty. Uncertainty by itself is not a barrier to good occupational and environmental health policy. Indeed it is more typical than not that scientists and policy makers must take definitive action in the face of uncertainty in order to protect the public health and welfare. However, the ability to act properly in the face of uncertainty requires that risk estimates have reasonably narrow zones of uncertainty and high degrees of reliability. The proposed method fails badly on both counts. It is fatally flawed and must not be allowed to drive public policy.

Uncertainty and Misclassification

The OSWER/Brattin/Crump method is a probability model that will inevitably describe risks with exceptionally large and unreasonable ranges of uncertainty. For example, when the 2003 version of this model was used by Drs. Berman and Crump the lung cancer potency factors for 15 epidemiology studies varied by a factor of 50, even after trying to adjust for fiber type and size. And the range of uncertainty calculated around each one of these study specific potency factors was from 10 to 100 fold. For mesothelioma the estimated potency factors varied by a factor of 30 after taking fiber type and size into account with the uncertainty around each potency factor ranging from 10 to over 400.¹¹

The OSWER/Brattin/Crump model is inherently one that presents results with a range of uncertainty. This is true even in the best of circumstances where all the underlying data are valid, consistent and reliable. But where the data are prone to error and inconsistency the problems are magnified many fold.

Misclassification is the most common serious problem with data in an epidemiological study and its effect is to make it more difficult or impossible to find a true risk. For example if a study examines the level of chemical exposure that causes asthma and the laboratory consistently gives air sample results that err on the low side, it will appear that lower levels of the chemical cause asthma than is really the case. If the laboratory consistently misclassifies on the high side the study will understate the true risk. If the

¹¹ Berman DW and Crump KS. Technical support document for a protocol to assess asbestos-related risk. EPA #9345.4-06, October 2003. p 7.60

laboratory is randomly wrong, sometimes high and sometimes low, it will falsely seem like there is no relationship at all between exposure and effect.

There are thus two fundamental problems with the asbestos risk assessment method. First, it is a mathematical model that always generates ranges of uncertainty. Second, this uncertainty model is going to be applied to a set of data from 24 epidemiological studies that is full of misclassification errors and is highly unreliable. If the data are sufficiently flawed even the most elegant model will not correct the problem. The problems with error and misclassification are so severe in this case that since 1986 the EPA and all of its contractors and expert reviewers have felt compelled to raise warnings about how these weaknesses will compromise the integrity of the results. For example, “one of the complications in performing these calculations is that there is uncertainty associated with the potency factors. Thus, there will be uncertainty in the calculated lifetime excess risk values.”¹² Or “it is very clear that there are errors in the cumulative exposure values...and that these errors may be substantial”¹³ And “it is necessary to extrapolate from the original estimates of concentration or cumulative exposure to the corresponding bin-specific values based on data from studies at other locations. It is important to emphasize that this is a substantial obstacle and source of uncertainty in the development of bin-specific potency factors.”¹⁴

There are two main types of misclassification in the asbestos epidemiology database: misclassification of exposures and misclassification of effects.

Misclassification of Exposures

The OSWER/Brattin/Crump proposal identifies 24 epidemiological studies of asbestos and cancer that provide enough data on cancer cases and asbestos exposure to do calculations on risk. However, the environmental samples were taken under many differing circumstances, using many methods and techniques, dating back to the 1930s to the 1950s for most of the studies. In some cases actual measurements were not made, but

¹² Brattin W. Proposed approach for estimation of bin-specific cancer potency factors for inhalation exposure to asbestos. EPA Office of Solid Waste and Emergency Response, April 23, 2008. p 80.

¹³ Brattin 2008 p 50

¹⁴ Brattin 2008 p 73.

exposures were estimated using professional judgment. The errors and inconsistencies in this huge database cannot be overstated. In fact the OSWER/Brattin/Crump proposal itself lists 9 separate ways that the exposure estimates are uncertain and an entire appendix to the report discusses uncertainty in more detail.

The sources of error and inconsistency include the following:

- Variability between studies and within studies in the way samples were gathered and prepared for analysis.
- Variability between studies and within studies in the analytical methods used to define, measure and count asbestos. Berman and Crump stated it this way in 2003: “Measurements...derived using different analytical techniques and methods can vary substantially and are not comparable. In fact, results can differ by two or three orders of magnitude.”¹⁵ According to Dodson and Hammar, “There are over 30 different ‘standard’ methods available for the analysis of asbestos in a variety of media.”¹⁶
- Lack of reliable and consistent quality control methods for laboratory performance. The National Voluntary Laboratory Accreditation Program, which today provides standards for testing and measurement of bulk and airborne asbestos samples in the United States, was not created until 1976.
- Use of area samples to estimate personal exposures. For example, “stationary air monitors were used at the Ontario plant until 1969... the use of stationary air monitors may tend to underestimate the true exposure level of workers...”¹⁷ In some cases it may also overestimate personal exposures.
- Use of data collected during one time period to estimate values in another time period. For example, “environmental hygiene surveys started in the mid 1950s... For earlier periods dust levels were estimated by the company industrial hygienist based

¹⁵ Berman and Crump 2003 p 4.11

¹⁶ Asbestos: Risk Assessment, Epidemiology and Health Effects, Ronald F. Dodson, Ph.D., Samuel P. Hammar, M.D. (eds.), Taylor & Francis Group, LLC (2006), at 9.

¹⁷ Brattin 2008 p A4-6

on knowledge of past plant operations and conditions... Oftentimes there was not enough information to estimate the dust level for each job.”¹⁸

- Use of data collected on one shift or one job to estimate values for other shifts or jobs.
- Lack of data on respiratory protection and local exhaust ventilation.
- Lack of data on unmeasured short duration peak exposures. The McDonald study on the South Carolina textile plant workers did not include measurements of “short-term but high level exposures that may have occurred during daily ‘blowing down’ and whipping of burlap bags in the dust house.”¹⁹
- Lack of history on smoking and other possible confounders. The Berry and Newhouse British friction products plant study did not collect enough data to evaluate smoking prevalence at all.²⁰
- Incomplete or misclassified work histories. As one example, “unrecorded movement of personnel between the mine and mill and the factory in Asbestos, Quebec was reported by Liddell et al. (1997) to occur frequently. This effect makes the exposure estimates more uncertain and may lead to exposure misclassification.”²¹
- Assumptions about exposures made in the absence of data. For example, in the British friction products plant there are no data on the relative amounts of crocidolite used, but since “the authors seem to imply that the contribution is small... a screening level value of 0.5% is assumed for the average fraction amphibole in the workplace... this value is considered to be quite uncertain.”²²
- Inappropriate use of surrogate data. Where the relative amounts of chrysotile and

¹⁸ Brattin 2008 p A3-4

¹⁹ Brattin 2008 p A2-10

²⁰ Brattin 2008 p A1-4

²¹ Brattin 2008 p A6-5

²² Brattin 2008 p A1-2

amphiboles in the air were not known from actual data in a particular study or from TEM measures in comparable locations, the authors used information on the relative amounts purchased or processed as a proxy for the relative amounts in the air.²³ There is no evidence presented to support this assumption and there is good reason from basic industrial hygiene principles to question its validity.

- Extrapolations from limited data. The draft appears to make the extreme assumption that all chrysotile is contaminated with amphiboles based on a 1990 study in which 28/81 or 35% of chrysotile samples were found to have trace tremolite. Using this assumption, the proposed method estimates an amphibole fraction and applies this to all the studies where exposure to pure chrysotile was reported.²⁴ Sensitivity analysis has not been done to evaluate the impact of this assumption, but it is likely that it will result in a reduced potency factor for chrysotile and mesothelioma.
- Applying the model to Superfund sites will add another layer of exposure misclassification.

Conversion Problems: Making Bad Data Worse

The raw data on exposures are marred in all the ways noted above. But the problem gets worse at each subsequent step. The mathematical model requires exposure data that provide asbestos fiber type, length and circumference, but none of the historic data were gathered with methods that collected this information. Therefore, the OSWER/Brattin/Crump approach requires that the old data be converted to new values as if the samples had been analyzed with modern transmission electron microscopes. There are two steps to the conversion procedure, both of which add more instability and uncertainty to the process.

First, many of the old samples were collected with midget impingers and analyzed with standard light microscopes. This gives a count of dust particles but not fibers. Since the

²³ Brattin 2008 p 74

²⁴ Brattin 2008 pp C-14, A2-2

early 1970s there have been several side-by-side tests in which midget impinger/light microscope dust counts are compared with results from samples collected on membrane filters and analyzed for fibers with phase contrast microscopes (PCM). These side-by-side tests generate multipliers that can be used convert the old dust counts to more modern fiber counts. Unfortunately, this conversion process just creates more exposure misclassification because “the correlation between fiber counts and total dust is sometimes poor within a plant...and generally poor between plants.”²⁵ Side-by-side studies have generated conversion factors ranging from 0.1 to 30, a 300-fold difference (with most of the results between 1 and 10).²⁶ The OSWER/Brattin/Crump approach arbitrarily uses a value of 3 based on what the authors thought was most typical, explaining “extrapolation from dust measurements to PCM-based exposure is certainly an uncertain step.”²⁷

Second, once all the data have been expressed as fiber counts they are still not in the form required by the OSWER/Brattin/Crump model. The model requires that all the exposure data be grouped into specific “bins” defined by specific fiber types, lengths and circumferences. However, none of the epidemiology studies measured fibers in this way, so another conversion becomes necessary. This conversion uses exposure data from three reports from the late 1970s and early 1980s in which asbestos samples were analyzed with transmission electron microscopy (TEM) that measures specific fiber types, lengths and circumferences. The proposed method requires a judgment about which of the epidemiology studies in the risk assessment were done in workplaces most similar to the ones where TEM measures have been made. This would determine which correction factors would be applied to the old data, making the assumption, for example, that fiber types and sizes in textile manufacturing facilities in the 1940s and 50s were the same as in similar but different facilities in the 1970s or 1980s. This assumption introduces yet another source of error, misclassification and uncertainty to the risk assessment process. As described in the proposal itself “it is apparent that use of TEM data measured in one location to represent the particle size distribution in another

²⁵ Burton and Crump p 5.2

²⁶ Brattin 2008 Table C-1

²⁷ Brattin 2008 p 72.

location is a source of uncertainty.”²⁸ Moreover, a careful reading of the proposal makes it clear that the actual conversion calculations will be even more prone to error because they will be based on undefined “other considerations” when there is no industry or operation similarity.²⁹

Even if exposure conditions in one time and place could be accurately matched to conditions in other times and places, the conversion from PCM fiber data to TEM exposure bins introduces another major error. “PCM and TEM results do not correlate well, and no generally applicable conversion factor exists between the two measurement techniques.”³⁰

Misclassification of Effects

Problems with certainty and reliability arise in epidemiology studies when the measures of effect (in this case cancer deaths) are subject to error or bias. This can come about in at least the following ways.

- Incomplete ascertainment of deaths in cohorts. In one example, a study of asbestos products retirees was limited to men who retired from the company. It did not include individuals who died or left employment before retirement. “This is a significant limitation to the data.”³¹ For some of the studies, incomplete follow-up with cohorts has meant large data gaps exist regarding additional potential deaths from lung cancer or mesothelioma. Twenty percent of the Swedish cement plant cohort, for example, was lost to follow up.³² The McDonald South Carolina textile plant study does not even report the percentage of the workforce that was lost to follow-up.³³ In addition, for many of the studies, women are excluded entirely from any follow-up analysis.

²⁸ Brattin 2008 p 76

²⁹ Brattin 2008 p 75

³⁰ OSHA Standard Interpretation letter 6/30/2005 from Assistant Secretary Jonathan Snare to U.S. Senator Conrad Burns.

³¹ Brattin 2008 P A3-3

³² Brattin 2008 p A12-2

³³ Brattin 2008 p A2-6

- Immature cohorts. For illness with long latency periods it is important that sufficient time has passed for dose-response effects to express themselves. Otherwise cases will be missed and risks underestimated. This will certainly be the case with the OSWER/Brattin/Crump analysis, because when most of the studies included were completed a majority of cohort members were still alive. For example, only 20-40% of the cohort members were deceased in the Albin, Yano, Neuberger, Hughes, McDonald (Connecticut), McDonald (Pennsylvania) and McDonald (South Carolina) studies. In several cases follow up studies were conducted that identified significant numbers of additional deaths but will be excluded from the OSWER/Brattin/Crump analysis because of incomplete exposure records. For example, there were 769 additional deaths in the follow up study by Berry and Newhouse and 162 deaths in the Enterline cohort follow up which will be excluded from analysis. The potential importance of these exclusions is illustrated by the recent update by Mirabelli of the Piolatto study of Italian chrysotile miners.³⁴ Two mesotheliomas were reported in the original study that ascertained deaths through 1987. Mirabelli found six additional mesotheliomas among cohort members who died between 1988 and 2006 (and five more among subcontractor employees). Similarly, when Wagoner, Robinson and Lemen first reported on deaths among their cohort of Manheim textile and friction product workers in 1971 there were no mesotheliomas, but when follow up was done through 1979 there were 17 mesotheliomas.³⁵ It is notable that one of the groups being excluded from OSWER/Brattin/Crump is the insulation cohort studied by Selikoff and colleagues. Mesotheliomas continued to appear as the group of New York and New Jersey insulators aged until 1992 when 95% were deceased.³⁶
- Small numbers of deaths or exposure measures for various times and places.
- Misdiagnosis of the cause of death. It has been well established that many cases of mesothelioma have historically been under-reported, undiagnosed, or misdiagnosed.

³⁴ Mirabelli D et al. Excess of mesotheliomas after exposure to chrysotile in Balangero, Italy. OEM Online First, 6/4/08 as 10.1136/oem.2007.037689

³⁵ Lemen R personal communication.

³⁶ Landrigan P et al. the hazards of chrysotile asbestos: A critical review. Ind Health 1999;37;271-280.

Death certificates have been notably unreliable, particularly before the 1960s, but even more recently because versions of the International Classification of Diseases (ICD) prior to the 10th edition (1999) did not classify mesothelioma separately, but only as “pleural cancer”. Very few studies have gone to the lengths taken by Selikoff and colleagues who made substantial efforts to obtain medical records and tissue specimens for review by pathologists. It is notable that while the Selikoff cohort, with its careful diagnostic validation, has been excluded from the OSWER/Brattin/Crump analysis, the Lacquet asbestos cement factor study, which is being included, is subject to enormous diagnostic error and bias. In that case cause of death was determined by interviews with family doctors “or social workers who visited relatives of the workers.”³⁷

When providing estimates of the total number of deaths caused by asbestos exposure between 1979 and 2001, the Environmental Working Group explained: “The data also grossly underestimate mesothelioma mortality, the signature asbestos-caused cancer. This is in part due to under-diagnoses of the disease, but in greater measure because mesothelioma was not tracked by the federal government as a cause of death until 1999. Prior to that, scientists estimated mesothelioma mortality by assuming cancers of certain sites (for example, the pleura) were mesothelioma. This resulted in dramatic underestimates of the true mortality rates. When the government began tracking mesothelioma as a cause of death, mortality more than doubled, from 935 in 1998, to 2343 in 1999.”³⁸

The OSWER/Brattin/Crump draft acknowledges probable diagnostic error but simply chooses to ignore it “because the magnitude of the error, if any, is unknown, and because the error is likely to be small...”³⁹ No evidence is provided to support this presumption.

³⁷ Brattin 2008 p A15-2

³⁸ http://reports.ewg.org/reports/asbestos/maps/government_data.php#moreinfo

³⁹ Brattin 2008 C-13.

- Decisions to exclude or ignore data. This is likely to have a significant impact on the results because the proposed model is extremely sensitive to the inclusion or exclusion of small numbers of studies or cancer cases.
 - As many as eight mesothelioma deaths reported by Henderson and Enterline (1979) are being excluded from the analysis because the study did not present “data on mesothelioma incidence as a function of cumulative exposure.”⁴⁰ However, “cumulative exposure estimates at the time of retirement were made for each worker”⁴¹ in the cohort, so it would seem that adequate data are available to include all the mesothelioma cases. This may be especially important because six of the eight were exposed primarily to chrysotile.
 - Twenty-five mesothelioma deaths from McDonald’s Quebec cohort have been excluded because cumulative exposure or time since first exposure could not be easily estimated.⁴² However, “cumulative exposures were estimated based on detailed work histories for each man in the cohort,” and the OSWER/Brattin/Crump draft describes a specific method for estimating cumulative exposure for these mesotheliomas⁴³ so this explanation makes little sense and is misleading.
 - Unpublished data from the Wittenoom, South Carolina and Quebec studies that were used in 2003 are now being excluded because EPA has not been able to make them publicly available. Only the published data from these cohorts will be used. EPA needs to either make the data available or evaluate and report on the impact of excluding these data.
 - Data on the large and “very important”⁴⁴ insulation worker cohort studied by Selikoff (1979) and Selikoff and Seidman (1991) were included in the 2003

⁴⁰ Brattin 2008 p A3-5

⁴¹ Brattin 2008 p A3-4

⁴² Brattin 2008 p A6-6

⁴³ Brattin 2008 p A-1 in Attachment 1 to Appendix A

⁴⁴ Brattin 2008 p 69

analysis but are now going to be excluded. This cohort includes information on more than 400 mesothelioma deaths, many of them among workers exposed only to chrysotile.^{45 46} This is clearly one of the most important sources of information available about asbestos and mesothelioma, but the new OSWER/Brattin/Crump proposal excludes this group because the “study population was not exposed at a single location but was composed of individuals from across the U.S. and Canada” and because “the asbestos content of insulation changed over time.”⁴⁷ However, the ability to estimate cumulative exposures for the insulation worker cohort is at least as good as for several of the studies that have been selected for inclusion. OSHA considered this criticism of the Selikoff study in 1986 and rejected it, stating “excluding this study would mean excluding 45% of all the asbestos-related lung cancer deaths and 84% of all the mesothelioma deaths from the overall analysis. OSHA believes it would be a serious error to eliminate such a large portion of the available data, when appropriate estimates of the exposure levels of these workers are available.”⁴⁸

- The Levin (1998) and Ohlson and Hogstedt (1985) studies were excluded because it would have been necessary to estimate cumulative exposure by using cohort wide mean concentrations and “workers with the highest exposure levels may tend to leave the workforce earliest.”⁴⁹ However, there is no evidence presented in support of this speculation.

- As noted above, an important update of the Piolatto cohort of Italian Chrysotile miners has been recently published that reports on 25 newly identified mesothelioma cases: four among mine workers, three among white collar mine employees, five among mine subcontractors, three among workers who processed the asbestos off site, and ten among people exposed to re-used mine tailings or

⁴⁵ Landrigan P et al. The hazards of chrysotile asbestos: A critical review. *Ind Health*. 1999;37;271-280.

⁴⁶ Nicholson W. The carcinogenicity of chrysotile asbestos – A review. *Ind Health*. 2001;39;57-64.

⁴⁷ Brattin 2008 p 69

⁴⁸ Preamble to OSHA Asbestos Standard 1986. 51 FR 22612

⁴⁹ Brattin 2008 p 69

other community exposures.⁵⁰ These cases are not included in the OSWER/Brattin/Crump proposal.

- Other potentially important studies were excluded without any mention or explanation. These include Cullen and Baloyi's study of Zimbabwe miners and Pira's cancer mortality study from an Italian asbestos textile plant.^{51 52} The Pira study is included in the proposal's reference list but will be excluded from the analysis, despite the fact that it provides detailed information on 37 pleural and peritoneal cancer and 222 lung cancer deaths.
- Three mesothelioma cases from the Hein cohort were excluded because the data were insufficient for computing incidence as a function of cumulative exposure.⁵³ However, there were cumulative exposure data for everyone in the study and all the lung cancer cases were included. Also, one mesothelioma case from the McDonald study of the same textile plant was included and McDonald apparently had the same exposure measurements to work with that Hein had.

There is no compelling scientific basis for estimating different potency factors for lung cancer by fiber type and OSWER should take bins that assume this off the table.

Stayner, Dankovic and Lemen have reasoned convincingly that “there is absolutely no epidemiologic or toxicologic evidence to support the argument that chrysotile asbestos is any less potent than other forms of asbestos for inducing lung cancer” and that “chrysotile appears to be just as potent a lung carcinogen as the other forms of asbestos.”⁵⁴ Berman and Crump cited supportive evidence for this in 2003, stating “at

⁵⁰ Mirabelli D et al. 2008.

⁵¹ Cullen M and Baloyi R. Chrysotile asbestos and health in Zimbabwe, I: analysis of miners and millers compensated for asbestos-related diseases since independence (1980). *Am J Ind Med.* 1991;22:531-542.

⁵² Pira E et al. Cancer mortality in a cohort of asbestos textile workers. *Brit J Cancer.* 2005;92:580-586.

⁵³ Brattin 2008 p A2-5.

⁵⁴ Stayner L et al. Occupational exposure to chrysotile asbestos and cancer risk: A review of the amphibole hypothesis. *Am J Public Health.* 1996;86:179-186.

least for lung tumor induction in rats, the best estimate is that chrysotile and the amphiboles are equipotent.”⁵⁵

OSWER has not validated its approach. It should not proceed further until doing so.

The failure to conduct sensitivity and goodness of fit analysis, and to make these analyses public, was a key criticism leveled by the 2003 expert panel. OSWER and its contractors have still not completed sensitivity analyses and goodness of fit evaluations recommended by the expert panel. However, a sensitivity analysis done in 2003 by one of the expert panel members showed that the entire modeling exercise was too unstable and unreliable to use for public health purposes. That analysis showed how the estimated potency factors for lung cancer can vary dramatically depending on small changes in the choice of studies included in the analysis. “When all epidemiological studies were considered in his analysis, the amphibole fibers were found to be three times more potent than the chrysotile fibers. When the cohort of chrysotile miners and millers from Quebec was omitted from this analysis, however, the amphibole fibers were found to be nearly two times *less* potent than the chrysotile fibers. Conversely, when the cohort of textile workers from South Carolina was omitted, the amphibole fibers were found to be more than ten times more potent than the chrysotile fibers. Given that the conclusions drawn about the relative potency of chrysotile and amphibole fibers appear to be highly sensitive to whether single studies are omitted from the analysis, this panelist was more skeptical about whether the increased potency of amphibole fibers is a robust finding. He recommended that the authors, when completing the proposed protocol, conduct similar sensitivity analyses to help reveal the factors or studies that appear to contribute most to lung cancer.”⁵⁶

⁵⁵ Berman and Crump 2003 p 6.124

⁵⁶ Eastern Research group 2003 p 3-4

OSWER plans the sensitivity testing only after the expert panel signs off on the proposed method,⁵⁷ but it is unreasonable to ask the Asbestos Committee to render judgments about the method before seeing these results. This is particularly true because the OSWER/Brattin/Crump proposal suggests they may use the sensitivity analysis to exclude data items that are “outliers” and have a particularly powerful and disproportionate impact on the results. While it is sometimes appropriate to remove outlier data that are likely to be fundamentally erroneous or corrupted, the outliers in this case may well be among the most important studies and cases. Excluding them because they will have an impact on the results would improperly allow the modeling method rather than the evidence to dictate the results. EPA should not proceed further with this exercise without conducting sensitivity analyses as recommended by the expert reviewers in 2003. The selective exclusion of relevant studies can only bias findings.

The draft indicates that OSWER has considered several ways to do goodness of fit analysis and suggests that it has actually tried some of them.⁵⁸ However, if it has done such a “goodness of fit” analysis it has not released the results or made them publicly available.

Why revisit work that was previously unsuccessful? Is there something new?

There have been no significant new studies or data since 2003 that would provide a compelling basis for another risk assessment proposal. All the reliability and certainty problems identified in 1986, 1989, 1999, 2001 and 2003 still exist. The latest proposed approach doesn’t do anything to eliminate or reduce these – they are inherent to the imperfect historic data and to the modeling method. The new approach ignores the inconsistencies, errors and biases in the data and masks them behind quantitative models which simply provide better statistical descriptions of some of the uncertainties than in

⁵⁷ Brattin 2008 p 3

⁵⁸ Brattin 2008 pp 57-58

2003. And in some cases, because of smaller bins, the range of uncertainty around specific estimated potencies will actually increase.

The new draft claims that “Since the derivation of the lung cancer and mesothelioma potency factors by USEPA (1986), evidence has accumulated that the toxicity and carcinogenicity of asbestos may depend both on mineral group or type (e.g., amphibole vs. chrysotile) and particle size (length, width) (e.g., Hodgson and Darnton 2000, ATSDR 2001).”⁵⁹ But these are review documents. They are not new evidence and EPA has not adopted them as such. And Hodgson and Darnton have warned about some of the major limitations of the data.⁶⁰

Of 261 references (not including statistical papers) in the OSWER/Brattin/Crump proposal only 22 (8%) were published since 2003 and with one exception these do not appear to provide significant new information. Only fourteen of these are original new research, the other eight being review papers. Of these fourteen, five are animal or laboratory toxicology studies (2 on apoptosis, 2 on oxidative stress, and 1 on genotoxicity). The remaining nine new papers are epidemiological studies. Two of these (Hein and McDonald) are updates of cohorts that were included in the 2003 analysis. The other seven are not going to be used - one each on gastrointestinal cancer, retroperitoneal fibrosis, mesothelioma incidence trends, x rays from the Libby population, environmental crocidolite, autoimmune disease, and cancer in a textile cohort. The latter paper, a cohort mortality study in an Italian asbestos textile plant,⁶¹ is the only new paper referenced that appears to provide significant new information about mesothelioma and lung cancer risk, but OSWER/Brattin/Crump plans to exclude it from consideration without any explanation.

⁵⁹ Brattin 2008 p 1

⁶⁰ Hodgson J and Darnton A. The quantitative risks of mesothelioma and lung cancer in relation to asbestos exposure. *Ann. occup. Hyg.* 44: 8; 565–601. “It is generally assumed that the most reliable guide to does specific risk is provided by exposure analyses using estimates of individual exposures. This is clearly the case when these individual exposure values can be accurately determined. However this assumption is very much not the case in the studies in this review. Not only are there the inevitable problems of extrapolating earlier exposures on the basis of more recent measurements; there are also problems of converting the most usual historic measurements (in terms of particle counts) to the more relevant measure of fibre counts. Direct fibre counting only became generally used in the 1970s.” p. 567

⁶¹ Pira E et al. Cancer mortality in a cohort of asbestos textile workers. 2005. *Brit J Cancer.* 92:580-586.

For the past twenty years the authors and expert reviewers of the various proposals for asbestos risk assessments have warned about the problems with data error, misclassification and uncertainty. But, despite this recognition EPA and its contractors continue to search for a “better” mathematical model. But when the new models are applied to the same, old and flawed database of asbestos exposure measurements the results remain unstable and unreliable. As Hodgson and Darnton have noted “ Faced with clearly discrepant data, purely statistical criteria cannot be used to decide on a ‘correct’ summary or compromise estimate.”⁶²

EPA and its contractors seem to feel comfortable with a model that generates results bounded by high degrees of uncertainty because they understand the underlying mathematics and believe the limitations will be apparent to anyone who reads the fine print. They apparently feel that as long as the problems with reliability and certainty are described, they are acceptable. However, the new approach is intended for practical use by non-experts. EPA plans to provide simple “spreadsheet tools” for applying the new potency values to calculate lifetime cancer risks. While this will make the estimates appear to be stable and “real,” it will mask the enormous problems known to the experts. This is a recipe for misinterpretation and misuse.

⁶² Hodgson and Darnton p 568

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