



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

October 29, 1984

Honorable William D. Ruckelshaus
Administrator
U. S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

OFFICE OF
THE ADMINISTRATOR

Dear Mr. Ruckelshaus:

On July 24, 1984, the Environmental Health Committee (EHC) of the Science Advisory Board reviewed two Agency documents on asbestos. These include:

- a draft document entitled "Asbestos Health Assessment Update," prepared by the Office of Health and Environmental Assessment in EPA's Office of Research and Development (ORD) [EPA-600/8-84-003A; February, 1984].
- a paper prepared by the Criteria and Standards Division in the Office of Drinking Water (ODW) and entitled "Major Issues Associated with Health Effects of Asbestos in Drinking Water (Carcinogenesis of Ingested Asbestos Fibers)."

Two scientists who are experts on the subject of asbestos assisted the Committee: Dr. Brooke T. Mossman from the University of Vermont and Dr. J. Corbitt McDonald from McGill University.

The purpose of the first document is to provide the health effects basis for possible revisions in the 1973 National Emission Standard for Asbestos (40: CFR §61.20, Subpart B). Key Committee findings and conclusions regarding the ORD update are summarized in the attached paper. The purpose of the second document is to address the question of whether or not there is a sufficient basis to conclude that ingestion of asbestos fibers increases the risk of gastrointestinal or other cancers in humans. A separate letter has been sent to Mr. Jack Ravan, Assistant Administrator for Water, concerning the ODW issue paper, which is also attached.

The Environmental Health Committee finds that the two documents contradict each other on a very important scientific issue. ORD's Health Assessment Update finds a consistent association between gastrointestinal cancer and exposure to airborne asbestos, presumably from swallowing the inhaled fibers brought up from the respiratory tract. The ODW analysis does not reach this conclusion.

The remainder of this letter summarizes three key points:

First, the EHC finds that the evidence available since 1972 increases the certainty that inhaled asbestos causes lung cancer and mesothelioma.

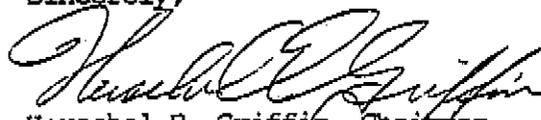
Second, the EHC agrees with the ODW issue paper that peer-reviewed experimental analyses of animal toxicology evidence does not support, at this time, an association between asbestos exposure and gastrointestinal cancer, whether by diet or by mucociliary clearance of inhaled fibers. ODW staff did, however, draw attention to a recent study from the National Toxicology Program (NTP), which has not yet been peer-reviewed or published. The NTP bioassay may contain evidence supporting the incidence of tumorigenesis by asbestos ingested by experimental animals. This conclusion has not been reached in other bioassays. Completion and peer-review of this study might resolve whether there is the possibility of an increased risk of gastrointestinal cancer in humans exposed to asbestos fibers from drinking water.

Third, both documents address the association between human exposure (particularly through ingestion) of asbestos and cancers other than those of the lung. Twelve of the thirteen epidemiologic studies reviewed in the ODW document reveal an apparent excess risk. A critical review of these thirteen studies, commissioned by EPA through its Center for Environmental Epidemiology at the University of Pittsburgh, concluded that no individual study or aggregation of these studies could be utilized to develop risk levels. While the agreement between the studies, or between the male and female populations within a study, was low, the association of cancers of the esophagus, stomach, pancreas or prostate were unlikely to have been generated by chance alone.

In summary, the Environmental Health Committee conclusion is that given the positive signal seen in the epidemiologic evidence, in addition to well-documented evidence for the association between asbestos fiber inhalation and lung cancer, it is hard to dismiss the possibility of an increased risk of gastrointestinal cancer in humans exposed to asbestos fibers from drinking water. However, the Committee consensus position is that the current peer-reviewed evidence from both animal and human studies does not support the view that the ingestion of asbestos from drinking water causes organ specific cancers.

More detailed technical comments from individual EHC members have been communicated directly to ORD and ODW. We greatly appreciate the opportunity to advise you on these scientific questions. The Committee is prepared to revisit the issues, if requested, when the new evidence can be evaluated.

Sincerely,



Herschel E. Griffin, Chairman
Environmental Health Committee



Norton Nelson, Chairman
Executive Committee

cc: Alvin L. Alm (A-101)
Joseph A. Cannon (ANR-443)
Bernard D. Goldstein (RD-672)
John A. Moore (TS-788)
Jack E. Ravan (WH-556)
Terry F. Yosie (A-101)

ENVIRONMENTAL HEALTH COMMITTEE KEY FINDINGS AND CONCLUSIONS
FOR THE DRAFT ASBESTOS HEALTH ASSESSMENT UPDATE [EPA -600/8-84-003A]

On July 24, 1984, the Environmental Health Committee (EHC) of the Science Advisory Board reviewed a draft document entitled "Asbestos Health Assessment Update," prepared by the Office of Health and Environmental Assessment (OHEA) in EPA's Office of Research and Development. The purpose of the document, as explained by the staff of OHEA and the the Office of Air Quality Planning and Standards, is to provide the health effects basis for possible revisions in the 1973 National Emission Standard for Asbestos.* In particular the document is meant to describe health effects information new since 1972 and to determine whether or not unit risk values for asbestos can be specified. The latter inquiry requires an analysis of the epidemiologic record for evidence of linearity of health response with exposure to asbestos.

The Committee's key findings and conclusions include:

First, nothing in the document persuades the Committee of any necessity to change the position set out in the 1973 emission standard that inhaled asbestos fibers are carcinogenic to the human lung. Instead, the literature examined supports the conclusions of the previous review that asbestos falls into the group 1 category ("... the chemical is carcinogenic to humans") of the International Agency for Research on cancer.

Second, the Committee finds that, for five issues identified below, the document should more thoroughly describe the recently available literature on the health effects of asbestos, so as to provide more complete descriptions of why certain scientific positions and rationales were adopted. In view of the deficiencies in the completeness of the literature review, the Committee did not look in much detail beyond these problems into the reasonableness of the judgments made. The five issues include:

(1) The type of asbestiform fiber:

As currently written, the calculated risks assume that all three kinds of commercially available asbestos (chrysotile, amosite and crocidolite) are the same with respect to pleural mesothelioma at a given exposure. In fact, many scientists do not agree with this view. Instead, they find that exposure to amphibole types (amosite and crocidolite) carries greater risk than for serpentine asbestos (chrysotile). The degree of this controversy should be discussed adequately for the regulator because most of studies analyzed in the document are for exposure to amphibole types. Environmental monitoring data are not good on this point, and some environmental exposure to amphibole types does occur, but most domestic environmental exposure is to chrysotile fibers. In addition, the document could better address the difference in risk with physical and chemical properties of the fibers.

* 40: CFR §61.20; Subpart B, National Emission Standard for Asbestos. See Federal Register 38: 8820 (1973) National emissions standards for hazardous pollutants, asbestos, beryllium and mercury.

(2) Exposure data:

The document gives greater weight in deriving a risk value to studies in which individual exposures were not estimated. In fact, epidemiologic studies are available in which individual exposures are estimated. In addition, the distribution of samples at a site generally adheres well to a log-normal distribution. The document, however, uses pooled samples from all sites, which assumes a similarity of sites and sources. These differences need to be emphasized for the regulator because any statistical bias in the description of the past incidents in which asbestos exposure was associated with health effects will be replicated in the prospective estimates of risk used in regulating.

(3) Mutagenesis by asbestos:

The document leaves an impression that asbestos fibers probably are weakly mutagenic, by citing a series of papers with positive experimental findings, but no summary conclusion is stated. In fact, more papers provide negative experimental results than not, but some of the negative evidence is not cited. While on the one hand some evidence may exist for aneuploidy caused by asbestos, on the other hand several scientists have reviewed this literature and concluded that asbestos probably is not mutagenic in the classic sense of causing gene mutations and/or chromosomal breakage. This controversy should be reviewed for the regulator because classic gene mutation should be reviewed for the regulator because classic gene mutation action by a substance generally is taken as supportive of an oncogenic mechanism involving a direct action of the substance or a metabolite of the substance on genes. Such mechanisms generally involve low dose linearity.

(4) The association between exposure to asbestos and cancers other than those of the lung (particularly the issue of gastrointestinal cancer following oral ingestion or inhalation):

The EHC finds that current peer-reviewed evidence does not support the view that ingested asbestos causes organ-specific cancers. The epidemiologic record is ambiguous. EPA has commissioned a critical review of thirteen (13) published and unpublished epidemiologic studies of cancer, caused by ingested asbestos in five areas of the U.S. and Canada, through the Agency's Center for Environmental Epidemiology at the University of Pittsburgh.† This critical review found a large variability in results among the studies, which was matched by discrepancies between data for male and female populations within the studies. Specifically, positive associations were jointly observed in both sexes in one of six studies of esophageal cancer, two of eight studies of stomach cancer and one of eight studies of pancreatic cancer. However, the positive associations that were observed for cancers of esophagus, stomach, pancreas or prostate, were unlikely to have been generated by chance alone.

† Gary M. Marsh, "Critical Review of Epidemiologic Studies Related to Ingested Asbestos," Environmental Health Perspectives 53 (1983), 49-56.

The variable results in the thirteen studies were attributed to several major factors:

- (a) differences in the characteristics of asbestos exposure between the study populations,
- (b) different study designs, and
- (c) a fundamental underlying weakness in that all of the studies relied on geographic correlations, which causes a substantial bias that can make an association look stronger or weaker than it is at the individual level.

The critical review recommends that a prioritized list of etiologic hypotheses should be tested at the more definitive individual level.

The peer-reviewed evidence from studies of experimental animals does not support, at this time, an association between asbestos exposure and gastrointestinal cancer, although a study from the National Toxicology Program (NTP) which has not been peer-reviewed recently became available. The NTP study may contain evidence in favor of tumorigenesis by ingested asbestos. If so, this issue bears reexamination. The possibility of differing interpretations of the literature for extrathoracic sites should be displayed for the regulator, because findings of carcinogenesis by routes of environmental exposure other than inhalation might necessitate different kinds of control actions.

(5) Linearity of lung tumor incidence:

The EHC advises that a risk assessment for lung cancer caused by asbestos inhalation is possible, but that the current draft document misses the mark, principally because uncertainty is not adequately expressed. For example, the document does not analyze data from three studies in which an effort was made to document the exposures of individuals. While these studies may provide more support for linearity than is present in the document, they also would reveal differing slopes in the relationship between asbestos exposure and lung cancer incidence. The variance in slope is an important uncertainty in making prospective estimates of risk, and it should be revealed to the regulator.



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OFFICE OF
THE ADMINISTRATOR

Mr. Jack E. Ravan
Assistant Administrator for Water [WH-556]
U. S. Environmental Protection Agency
401 M Street, SW
Washington, D.C. 20460

Dear Mr. Ravan:

On July 24, 1984, the Environmental Health Committee (EHC) of EPA's Science Advisory Board reviewed a paper prepared by the Criteria and Standards Division in the Office of Drinking Water (ODW) and entitled "Major Issues Associated with Health Effects of Asbestos in Drinking Water (Carcinogenesis of Ingested Asbestos Fibers)." Two scientists who are experts on the subject of asbestos assisted the committee: Dr. Brooke T. Mossman from the University of Vermont and Dr. J. Corbitt McDonald from McGill University.

The scientific issues presented to the Committee for its review were carefully framed. The document with its supporting material was well-focused and reached the Committee in a timely way. Unlike the clarity with which your staff presented the key scientific issues, to date little of the relevant evidence is amenable to clear-cut scientific interpretation.

Regarding experimental animal evidence, ODW staff drew attention to a recent study from the National Toxicology Program (NTP), which has not yet been peer-reviewed or published. The NTP bioassay may contain evidence in favor of tumorigenesis by asbestos ingested by experimental animals, a result which has not been reported in other bioassays. The Committee is prepared to revisit the issues when this evidence can be more widely evaluated. It understands that ODW staff have transmitted a copy of the bioassay to EPA's Carcinogen Assessment Group for their evaluation. Otherwise, the EHC agrees with ODW's assessment that the animal toxicologic evidence should be considered negative with respect to any association between ingested asbestos fibers and gastrointestinal cancer. Thus, peer-reviewed experimental analyses of hazard does not support, at this time, an association between asbestos exposure and gastrointestinal cancer, whether by diet or by muco-ciliary clearance of inhaled fibers.

In contrast, the epidemiologic record is ambiguous. As compared to the thirteen (13) studies reviewed by ODW staff, Dr. McDonald cited some thirty (30) studies, of which eighteen (18) suggest the possibility of a positive association. Some good reasons exist for the inconsistency of the evidence. These include:

- ° in some instances it is not clear what was the nature of the asbestiform material that was the source of the exposures.
- ° the studies were conducted with small populations at high exposure to a putatively low risk material.
- ° tumor site may be recorded ambiguously (for example, lower and upper gastrointestinal tract sites may or may not have been analyzed separately).
- ° the association resembles that seen with other materials that act as confounding factors rather than as causative agents.

Twelve (12) of the thirteen (13) epidemiologic studies reviewed in the ODW document reveal an apparent excess risk. The same thirteen studies were the subject of a critical review of health effects caused by asbestos ingestion that was commissioned by EPA through its Center for Environmental Epidemiology at the University of Pittsburgh.* The critical review concluded that each study had methodologic weaknesses and limitations, and that no individual study or aggregation of studies could establish risk levels. While the agreement between male and female populations within the studies was low, the association of cancers of the esophagus, stomach, prostate, and pancreas with asbestos ingestion was not likely to result from chance alone.

Although a poor quality risk estimate will result from such data, the population risk will be low, and some scientists prefer to work with such a risk estimate. Ambiguity exists in the epidemiologic record, and the draft report by the National Academy of Sciences Committee on Non-Occupational Health Risks of Asbestiform Fibers,† found that existing data do not provide a scientific basis to determine whether or not there is an association between ingested asbestos fibers and gastrointestinal cancer.

Given the positive signal seen in some epidemiologic studies, plus well-documented evidence for the association between asbestos fiber inhalation and lung cancer, it is hard for the Committee to feel comfortable in dismissing the possibility of an increased risk of gastrointestinal cancer in humans exposed to asbestos fibers from drinking water. However, the Committee consensus is that current peer-reviewed evidence for humans and animals does not support the view that asbestos ingested in water causes organ-specific cancers.

*Gary M. Marsh, "Critical Review of Epidemiologic Studies Related to Ingested Asbestos," Environmental Health Perspectives, 53 (1983), 49-56.

†National Academy of Sciences. Committee on Non-Occupational Health Risks of Asbestiform Fibers. Asbestiform Fibers: Non-Occupational Health Risks. National Academy Press, Washington, D.C., 1984.

More detailed technical comments from individual EHC members have been communicated directly to Dr. Cotruvo. We greatly appreciate both the opportunity to review the paper and to acknowledge the thoughtful consideration of the Committee's time.

Sincerely,


Herschel E. Griffin, Chairman
Environmental Health Committee


Norton Nelson, Chairman
Executive Committee

cc: Alvin L. Alm [A-101]
Joseph Cotruvo [WH-550]
Victor J. Kimm [WH-550]
Terry F. Yosie [A-101]