Appendix C-1
Risk Assessment:
Human Health and Environmental Impacts of Exposure to Environmental Asbestos

TOXICITY PROFILE FOR ASBESTOS

1.0 EXECUTIVE SUMMARY

Health risks associated with environmental exposure to ambient asbestos fibers are of potential concern because of reported adverse effects from occupational exposure and because asbestos, as well as other mineral and synthetic particles with similar properties, is present in the environment. This toxicity profile on asbestos reviews available asbestos studies and regulatory support documents to develop a set of recommended health criteria for exposure to asbestos via inhalation and ingestion. Major findings and recommendations are as follows:

- The most significant route of exposure to asbestos fibers is usually via inhalation. Additionally, ingestion of asbestos can occur either directly (e.g., drinking water) or indirectly following inhalation.

- Although identification of the biologically active components (e.g., fractions characterized by length, diameter, or aspect ratio) of asbestos have not been conclusively defined, there is evidence that the most biologically active fibers are those with length >5 microns and aspect ratio >3. Shorter fibers, however, also appear to contribute to health impacts. To adequately characterize asbestos concentrations, transmission electron microscopy (TEM) is recommended. Comparison with existing health studies for which measurements were made by other methods requires careful consideration of conversion factors.

- Generally, concentrations in ambient air are reported as fibers per unit volume (f/ml) or fiber mass per unit volume ($\mu g/m^3$); reported concentrations are usually linked to fibers >5 microns in length and/or with certain microscopic characteristics.

- Assessment of exposure is complicated by uncertainties in current measurement techniques, as well as in the conversion factors among the measures of concentration obtained by various methods.

- For measurement of asbestos at hazardous waste sites, it is important that the analytical method used be sensitive, rapid, able to differentiate between asbestos and nonasbestos fibers, and be cost-effective.

- The carcinogenicity of asbestos following inhalation has been clearly established in humans and experimental animals. In humans, such evidence comes from occupationally exposed individuals. Inhalation exposure to asbestos can result in both lung cancer and mesothelioma.

- The carcinogenicity of asbestos following ingestion has not been conclusively demonstrated by direct studies; however, increases in gastrointestinal cancer in a number of cohorts of occupationally

2.0 INTRODUCTION

Asbestos is a generic term referring to a family of naturally occurring hydrated silicates having a fibrous crystalline structure. Only six fibrous silicates are defined as asbestos fibers, and these fibers are classified under two basic mineral types, serpentine and amphibole. Chrysotile fibers belong to the serpentine group; actinolite, Cunningtonite-grunerite or amosite, anthophyllite, crocidolite, and tremolite fibers belong to the amphibole group. Chyrsotile fibers are composed of fibrils that are banded together. Each fibril is actually a rolled sheet of magnesium oxide-hydroxide octahedra bonded to a layer of silicon dioxide tetrahedra. Amphibole fibers consist of double chains of silicon-oxygen tetrahedra lying parallel to the vertical crystallographic axis and bound laterally by metallic ions (Selikoff and Lee 1978). Asbestos fibers are widely used for their high tensile strength and flexibility and for their noncombustible, nonconducting, and chemical-resistant properties. Chrysotile, amosite, anthophyllite, and crocidolite are of primary commercial importance, and therefore, most data exist for these fiber types.

Several of the physical and chemical properties of asbestiform fibers appear to be associated with causing adverse health effects. Longer, thinner fibers appear to be more pathogenic than shorter, thicker fibers. This particular fiber characteristic can be expressed quantitatively as the aspect ratio (i.e., the ratio of fiber length to fiber diameter). Other fiber characteristics that may be significant in pathogenicity include respirability (behavior of the fiber in the lung), durability, surface area, and surface chemistry. Health effects also appear better correlated with total fiber number than with asbestos mass, although limitations in the analytical techniques used to quantify asbestos concentrations color this observation.

This profile presents an assessment of health risks posed to the general population by low concentrations of asbestos present in the environment. The primary effects associated with exposure to asbestos are cancer (specifically lung cancer and mesothelioma) and asbestosis, which is characterized by fibrosis of the lung parenchyma. However, asbestosis is primarily observed in

3.0 ESTIMATES OF EXPOSURE

There are a number of different pathways by which asbestos can be released from a source and transported to points of potential exposure. Two of the most important pathways include (1) suspension in ambient air and subsequent airborne transport to exposure points followed by inhalation or inadvertent ingestion, and (2) release to water and subsequent aquatic transport to exposure points followed by ingestion. Potential receptors at environmental exposure points include humans and other local biota.

In humans, the primary route of exposure to asbestos fibers in air is via inhalation. Some of the inhaled fibers also can be translocated to the gastrointestinal tract by airway clearance mechanisms, and other fibers can be translocated to the pleural and peritoneal cavities by lymphatic drainage. Inhalation exposure can fall into the following four categories: (1) occupational, (2) community (near known sources), (3) consumer (use of manufactured products), and (4) general environmental. Because the highest asbestos exposures have been reported for relatively well-defined workplace populations, occupational exposure data are most frequently used in health hazard assessments for inhalation.

Ingestion is another potential route of exposure. Ingestion of asbestos can occur directly through the consumption of contaminated water, food, beverages, or soil, or ingestion can occur indirectly following inhalation of fibers because the exposed person can swallow nasal and bronchial secretions containing inhaled asbestos fibers.

The proper characterization of asbestos exposures requires structural and chemical information in addition to quantifying the concentration of fibers. Because of the variability in the characteristic properties of asbestos fibers, their detection and identification can often be difficult. Several methods have been developed for the identification and quantification of asbestos in air, water, and biological materials. Generally, asbestos concentrations are expressed as fibers per unit volume (f/ml) or fiber mass per unit volume

In addition, two other pulmonary mechanisms may protect against asbestos toxicity, formation of asbestos bodies and long-term *in situ* fiber degradation. Approximately 10-30% of asbestos fibers retained in human lungs become coated with hemosiderin and mucopolysaccharide to form yellow-to-brown structures called asbestos bodies (Schneiderman et al. 1981). Asbestos bodies are believed to be created by lung macrophages and appear to exert a protective effect against fibrosis (Morgan and Seaton 1984). *In situ* fiber degradation appears to be effective primarily for chrysotile asbestos. Chrysotile has a tendency to partially dissolve in weakly acidic solutions, which can facilitate clearance from the lung (Morgan and Seaton 1984). The effects of asbestos fibers and asbestos bodies are not limited to one target organ; they have been found in almost every extrapulmonary tissue.

The length of asbestos fibers appears to play an important part in determining biological activity. The predominant fibers found in the lung parenchyma and in extrapulmonary organs are those shorter than 5 microns in length. However, in case of asbestosis, peribronchial and perivascular lesions generally contain both long and short fibers. Current data indicate that both long and short fibers may be biologically active to some extent and are suspect in producing human disease (Schneiderman et al. 1981). It has been suggested that the biological activity of longer fibers (75 μm) may be due to the inability of macrophages to completely engulf the fiber. Damage of the macrophage cellular membrane may cause a loss of macrophage mobility and lead to release of lysosomal enzymes and oxygen free-radicals from the macrophage, which in turn may damage alveolar epithelial cells and initiate fibrosis. In addition, the longer fibers may disrupt the normal proliferation and differentiation of lung fibroblasts either as a result of interacting directly with the fibroblast or as a result of macrophage secretions (CDHS 1986, OSHA 1986). It has been suggested that fibers less than 5 microns in length may be completely phagocytized *in vivo*, whereas those longer than 25 microns generally are not. Those fibers in the intermediate range may be only partially phagocytized or may cause thinning of the phagosomal membrane (Langer et al. 1974). Short fibers tend to be translocated more readily than long fibers and should

Although the "Stanton hypothesis" appears to have been generally accepted, its limitations also have been noted. First, it was developed as a model only for mesothelioma, although it also may be applicable to other asbestos-induced tumors. Second, Stanton et al. (1981) noted that narrow dimensional ranges of sized fibers were not available for study, that errors in the measurement of asbestos fibers were unavoidable because of clumping and fragmentation, and that fine chrysotile fibers were not studied because they could not be measured analytically with precision. Third, a critical fiber length below which there would be no carcinogenic activity has not been demonstrated. Fourth, whereas clearance of fibers shorter than 5 microns is more efficient than for longer fibers, such clearance is neither instantaneous nor total, permitting shorter fibers to interact for substantial periods with pulmonary and pleural cells. Fifth, most asbestos fibers found in the pleura are short (<5 microns) fine chrysotile, whereas mixed fiber types are found generally in the lung parenchyma. Finally, although fiber dimensions clearly affect carcinogenicity, the relationship of physical dimensions to deposition and translocation to the pleura and peritoneum in humans has not been well characterized (CDHS 1986).

In addition to fiber dimension, it has been suggested by some investigators that surface chemistry of asbestos fibers may be an important determinant of disease (OSHA 1986). Asbestos-induced cytotoxicity has been found to be initiated by the reaction of the fiber with the plasma membrane of respiratory epithelial cells (Mossman 1983). Some studies have suggested that recognition of asbestos fibers by phagocytes and their subsequent phagocytosis may be due to physicochemical affinities between the fiber and the phagocyte (OSHA 1986).

It has also been reported that modification of the fiber structure may affect biological reactivity of the asbestos fiber. Results of one study indicated that ball milling of experimental asbestos samples resulted in important changes in the structural and surface characteristics of asbestos fibers, which reportedly reduced their effect on cell membranes. Results of other studies have indicated that milling procedures change not only the size distribution, but also the shape and crystal structure of asbestos fibers (OSHA 1986).

It should be emphasized that there is still considerable controversy s whether or not crocidolite or other amphibole asbestos types are more carcinogenic than chrysotile (EPA 1986). Great Britain, Canada, and Sweden, for example, have imposed far more rigid standards for crocidolite than other varieties of asbestos. In contrast, the United States has no special standard for any specific asbestos mineral. The question of fiber type was not addressed until the mid-1960's because analytical techniques used in epidemiological studies were unable to accurately characterize asbestos fiber types. This lack of information on fiber exposure by mineral type was recognized at the time of the 1964 New York Academy of Sciences Conference on Asbestos (Whipple and van Reyen 1965), and a recommendation was made that the importance of fiber type on the risk of developing asbestosis, carcinoma of the lung, and mesothelial tumors be investigated. In the ensuing years, considerable information was developed on the mortality experience of different groups exposed to different varieties of asbestos in different work processes. Unfortunately, the differential risk associated with different fiber types is still not completely understood (EPA 1986).

3.1.2 INGESTION

Specific data relating individual asbestos species and physical characteristics with biological activity via ingestion are lacking. Results of bioassays of amosite asbestos (McConnell 1983a,b) showed no evidence of carcinogenicity in experimental animals. Results of an NTP (1984) bioassay in rats provided some evidence that chrysotile fibers >10 microns in length, but not fibers <10 microns in length, may have some carcinogenic potential for the gastrointestinal tract. Results of a number of epidemiological studies of humans exposed to asbestos in drinking water, as reported by EPA (1985a), are inconclusive and provide no insight into identifying biologically active size fractions or mineral species of asbestos.

3.2.1 COLLECTION TECHNIQUES

Collection of mineral particles for identification and counting is usually done by filtering the medium (air or water) through mixed cellulose ester (MCE) membrane (Millipore®) or perforated polycarbonate (Nucleopore®) filters, thereby concentrating them through deposition on the filter's surface. The effective minimum particle collection size in each of the membrane or collection techniques is less than 0.5 microns (Rudd 1978).

It should also be noted that collection of air samples for asbestos analysis poses special problems associated with the type of temporal sampling protocol employed. Elevated airborne concentrations of asbestos tend to be the result of episodic rather than continuous release processes. Consequently, sampling over a relatively short time period may give misleading results. Air sampling results may be more useful if more aggressive sampling techniques are used. For example, it may be possible to simulate conditions likely to produce worst case asbestos exposures and to sample the air during these times.

Handling of samples after collection may pose significant technical problems. For example, asbestos in aqueous samples may adhere to receptacles in which they are collected, and asbestos in airborne samples may cling to the filter cassette walls because of static charges; this can result in an overall underestimation of the asbestos fibers present. Conversely, disruption of dry or wet fibers during handling and transport may break the asbestos fibers present into more numerous, shorter or thinner fibers, which could result in an underestimate or overestimate of the asbestos fibers present depending on the sensitivity of the analytical technique used.

3.2.2 SAMPLE PREPARATION TECHNIQUES

To prepare samples for examination with a phase contrast light microscope (PCM), impingement, impaction, thermal precipitation, or membrane filter techniques are used. Particles deposited directly on microscope slides by impaction or thermal precipitation can be counted by light microscopy. However, a more even dispersion can be obtained by impinging a jet of

3.2.3 MASS AND COUNTING MEASUREMENT METHODS

Table 3-1 presents the major analytical methods used in the quantification and identification of asbestiform fibers. The two major measurement methods include mass and counting techniques. The earliest methods measured mass. In the gross mass (gravimetric) methods, airborne dust was collected by filtration, precipitation, or impaction, and the total dust was determined by weighing on analytical balances. X-ray diffraction techniques were used to identify mineral types present in the dust and magnesium analysis was used as an index of chrysotile asbestos content. When there was a need to collect and measure samples over short times, such as in the evaluation of controls or brief exposure episodes, the mass of the small amount of material could be measured by very sensitive piezoelectric or beta-absorption instruments (NRC 1983a).

Major drawbacks to these early analytical methods were the insensitivity of the x-ray method in the detection of small particles, the nonspecificity in the differentiation of chrysotile from other serpentine minerals, and the similar nonspecificity of the magnesium assay. Because much of the mass measured by gross mass methods consisted of particles too large to penetrate into the lung, techniques were often used to remove the larger particles before assay. The horizontal, parallel plate elutriator was preferred in the United Kingdom, whereas industrial hygienists in the United States tended to use small cyclone devices (NRC 1983a).

It should be noted that mass measurements account for all sizes of asbestos. Although there may be fibers of relatively small size, if sufficient numbers are present, these small fibers may add significantly to mass concentrations.

Counting methods are far more sensitive than mass determinations, since samples with too little mass to be weighed are usually adequate for counting by certain methods. Furthermore, since small particles far outnumber large particles, counting emphasizes the respirable dust. Lastly, fibers can be counted separately from other particles (NRC 1983a).

Results of impinger counts are usually expressed in millions of particles per cubic foot; dust concentrations measured by other methods are typically expressed as particles or fibers per cubic centimeter. In some electron microscope techniques, fibers or dispersed fibrils are counted, and the results are then converted to units of mass per volume (NRC 1983a). A number of investigators have attempted to develop conversion factors for estimating the relative equivalency of different asbestos measurement methods that have been used in occupational settings. These relationships, as summarized in the NRC's (1983a) report on Asbestiform Fibers, are shown in Table 3-2. NRC (1983a) noted that the accuracy of the estimates is unknown, but is probably valid within about one order of magnitude. However, the conversion factors would be equivalent only in that they represent values that would be expected if paired measurements using different measurement techniques were made in an environment similar to that in which the conversion data were originally obtained.

3.2.4 QUANTIFICATION TECHNIQUES

Four major analytical methods are used for quantifying asbestos fibers: phase contrast light microscopy (PCM), polarized light microscopy (PLM), transmission electron microscopy (TEM), and scanning electron microscopy (SEM). PCM, which measures fibers per unit volume, has traditionally been used for counting fibers in the workplace. It has been used to measure fiber concentrations for fibers longer than 5 microns with a diameter of greater than 0.2–0.3 microns (the limit of resolution). Thus, fibers longer than 5 microns, but with diameters less than 0.2 microns, are not counted. Although fibers shorter than 5 microns with a diameter sufficient to be resolved may also be counted by this technique, a 5-micron cutoff has traditionally been employed when counting asbestos fibers by this technique. Additionally, PCM cannot distinguish asbestos from nonasbestos fibers of similar size and shape. Compared TEM and SEM, PCM is the least expensive, the most readily available, and involves the least sample preparation time (EPA 1985b). Although PCM is a practical technique for these reasons for routine use in the occupational environment, the method is too insensitive and nonspecific to be used to assess fiber exposure in the nonoccupational environment (NRC 1983a). It should be noted,

however, that PCM has generally been the technique used for exposure and risk estimates from which dose-response assessments are derived.

A second optical microscope technique, polarized light microscopy (PLM), suffers from some of the same limitations as PCM. It is predominantly limited to analysis of asbestos in bulk samples such as soil or rock. Among the advantages of PLM are sensitivity, rapidity, and the ability to identify the individual amphiboles. EPA has promulgated an official tentative method for PLM asbestos determination (40 CFR Part 763, Appendix A). Quantification is accomplished by counting the number of points on a superimposed reticle occupied by asbestos. The results are reported as area percent derived by dividing the number of points that contain asbestos by the total number of points. If three or fewer points are counted, the results from the standard 400-point grid are reported as <1% asbestos; thus, the quantification limit can be taken as four fibers in a sample.

Transmission electron microscopy (TEM) is most useful for measurements of asbestos in the ambient environment, where sensitive determinations of low concentrations are required. Quantification of samples with the newer TEM techniques yields estimates of fiber number, which can be converted to mass estimates, and allows greater resolution than the optical PCM technique. TEM has a resolution of 1 to 3 orders of magnitude more fibers than PCM techniques (OSHA 1986, EPA 1986). Consequently, counts based on TEM measurements are often more than 100 times greater than counts obtained by optical light microscopy (NRC 1983a). This includes fibers greater than 5 microns in length, thinner fibers (down to 0.25 nm in diameter), as well as total fibers (where TEM can resolve shorter fibers than PCM). TEM can be used to indicate the likely presence of asbestos in a population of fibers based on fiber shape and configuration alone. However, in order to confirm the identity of the fibers, chemical and/or crystal analysis is needed. Two identification techniques used with TEM are energy dispersive x-ray spectrometry (EDXA) and selective area electron diffraction (SAED). Although TEM is more sensitive to thin fibers and more specific for asbestos relative to PCM, it is less widely available, more costly, and involves more preparation and analysis time than PCM (EPA 1985b).

TEM-observed object in order to be seen. In terms of fiber dimensions, the limit of resolution obtained with SEM is a fiber diameter of 0.20 microns. SEM is less powerful than TEM in its ability to distinguish asbestos from other types of fibers; however, it is superior to PCM in its specificity for asbestos (EPA 1985b). Although the direct sample preparation method used for SEM provides little opportunity for contamination, the image resolution, contrast, and x-ray resolution of SEM have not been sufficient for precise mineralogical identification (NRC 1983a). Unlike PCM and TEM, no standardized protocol for sample preparation and analysis using SEM is currently available. Without standardized protocols, it is not possible to characterize analytical accuracy and reliability of SEM results. SEM analysis is generally more widely available than TEM, but less available than PCM. In addition, both cost and time of analysis using SEM are intermediate between PCM and TEM (EPA 1985b).

3.2.5 CONCLUSION

The ideal analytical method for asbestos should measure a characteristic, parameter, or index with biological relevance—that is, the measurement should be related to the risk of the disease end point being studied. Possible types of measurements might include, but not necessarily be limited to fiber number, mass, length, diameter, and mineral type. Because of evolution in understanding of asbestos toxicity, parameters that actually correlate with toxicity may not have been measured in past studies. Furthermore, standardization among sample preparation methods and analytical techniques are needed in order to allow comparisons of data from various laboratories. Much of the occupational exposure data on which current health risk estimates are based have been obtained using optical microscopy techniques. These techniques, however, are limited in their ability to identify specific types of asbestos fibers and to resolve short or thin fibers. Electron microscopy techniques, although more expensive, provide superior results with regard to characterization of fiber types and visualization of smaller fibers. Although it is currently thought that asbestos fibers greater than 5 microns in length are more biologically active than shorter fibers, the relative potency of different size fractions of asbestos has not been well characterized. One encouraging trend is the increasing use of TEM as the technique of choice when

TABLE 3-3

EMPIRICAL RELATIONSHIPS BETWEEN OPTICAL FIBER COUNTS AND MASS CONCENTRATIONS OF AIRBORNE CHRYSOTILE

Sampling Situation	Fiber[a] Counts (f/ml)	Mass Concentration ($\mu g/m^3$)	Conversion Factors $\frac{\mu g/m^3}{f/ml}$ or pg/f
Textile factory: British Occupational Hygiene Society (1968) (weight vs. fiber count)	2	120	60 16
Air chamber monitoring: Davis et al. (1978)	1950	10,000	5
Monitoring brake repair work: Rohl et al. (1976) Electron Microscopy (EM mass vs. fiber count)	0.1 to 4.7 (7 samples)	0.1 to 6.6	0.7 to 24[b] mean = 6
Textile mill: Lynch et al. (1970)			150[c]
Friction products manufacturing: Lynch et al. (1970)			70[c]
Pipe manufacturing Lynch et al. (1970)			45[c]

[a]All fiber counts used phase-contrast microscopy and enumerated fibers longer than 5 microns.

[b]Conversion factor may be low due to losses in electron microscopy processing.

[c]Conversion factor may be high because of overestimate of asbestos mass on the basis of total magnesium.

Source: EPA (1986).

deviations of 45% are not unusual in light microscope counts. In addition, measurements made in a particular environment at different times will vary because the actual concentrations vary. Second, the different techniques measure a variety of indices, which often do not remain in constant proportion to each other from sample to sample. For example, PCM fibers longer than 5 microns are counted as a single species, whereas shorter fibers are not counted at all. Therefore, a given fiber count obtained by this technique would undoubtedly represent a very different number of fibers and mass concentrations than the same fiber count obtained by electron microscopy. In some cases, reproducible conversion factors may be determined when large numbers of paired samples are analyzed by the various methods. However, these conversion factors usually cannot then be applied to samples obtained under a different set of conditions (NRC 1983a). Third, sample preparation techniques that are employed in electron microscopy can result in alterations in fiber size distribution. This in turn can lead to variability in proposed conversion factors (Schneiderman et al. 1981).

As suggested by this discussion, there is no universally accepted conversion factor (Schneiderman et al. 1983a). Further, conversion factors may not be applicable to samples obtained under different sets of conditions (NRC 1983a), and different conversion factors may be appropriate for crocidolite, chrysotile, and amosite asbestos (Rowe and Springer 1986). For risk assessment purposes, however, it should be recognized that the uncertainty associated with the use of conversion factors may be no greater than the uncertainty in other areas of the assessment.

3.4 ESTIMATES OF ENVIRONMENTAL EXPOSURE

Nicholson (1987) recently reviewed the extent of airborne asbestos occurrence in the nonoccupational environment. He noted that (aside from hazardous waste sites) the greatest ambient airborne exposures result from friable asbestos containing building materials. Table 3-4, reproduced from Nicholson (1987), tabulates the literature on ambient exposure levels. The State of California (CDHS 1986) has also reported ambient levels of asbestos ranging from 8 to 500 fibers/m^3. Lower levels of 8 to 80 fibers/m^3 were found at sites isolated

from known sources whereas higher levels of 50 to 500 fibers/m^3 were measured close to localized known sources.

4.0 DESCRIPTION OF HEALTH EFFECTS IN HUMANS

The carcinogenicity of asbestos following inhalation exposure has been clearly established in humans and experimental animals; the evidence in humans comes from data on occupationally exposed individuals (IARC 1977, NRC 1984, EPA 1986). Inhalation exposure to asbestos can result in lung cancer and mesothelioma (EPA 1986). The carcinogenicity of asbestos following ingestion has not been conclusively established; however there is available data from occupational studies that suggest a link between inhalation and subsequent ingestion of asbestos and gastrointestinal cancer. The primary noncarcinogenic health effect of asbestos in asbestosis, a chronic lung disease associated with functional disabilities and early mortality; however development of asbestosis is associated only with high-level occupational exposure.

4.1 CARCINOGENIC EFFECTS

Asbestos is recognized as carcinogenic to humans by the International Agency for Research on Cancer (IARC 1977) and by the Environmental Protection Agency (EPA 1985a). The strongest evidence for the carcinogenicity of asbestos in humans comes from epidemiological studies of occupationally exposed individuals. These studies have consistently linked exposure to asbestos with increased incidences of lung cancer and pleural and peritoneal mesothelioma. Several studies also have shown significantly increased cancer risks at other sites, particularly the gastrointestinal (GI) tract. The consistency and magnitude of the excess risks observed at these extrathoracic sites, however, are not as great as the risks for lung cancer and mesothelioma (EPA 1986).

A limited number of studies have suggested a possible association between increased incidence of human cancers and exposure to asbestos in nonoccupational settings. These studies have examined the occurrence of asbestos-related disease among family contacts of asbestos workers, residents living in the vicinity of asbestos facilities or other sources of ambient asbestos, and individuals living in areas where the drinking water supplies are known to contain relatively high concentrations of asbestos. However, these

TABLE 4-1
OBSERVED AND EXPECTED DEATHS FROM ALL CAUSES, LUNG CANCER, GASTROINTESTINAL CANCER, AND MESOTHELIOMA IN 41 ASBESTOS-EXPOSED COHORTS

Fiber Type and Study	Sex	COHORT Total Number	% Untraced	Years[a] of Follow-up	Years[b] from Onset	ALL DEATHS Obs.	Exp.	SMR[c]	LUNG CANCER[d] Obs.	Exp.	SMR	GI CANCER[d] Obs.	Exp.	SMR	Number of Mesotheliomas Pleural	Peritoneal	Unspec.	Other Cancers in Excess*
Chrysotile																		
Acheson et al. (1982)[e]	F	570	0.9	1951-80	10+	177	148.5	119	6	4.5	133	4	4.9	82	1	0		
Dement et al. (1983a,b)[e,g]	M	1261	2.1	1940-75	15+	245	152.5	161	33	9.8	336*	10	8.1	124	0	1		
McDonald et al. (1983a,b)[e,g]	M	2543		1938-77	20+	570	447.0	127	59	29.6	200*	26	17.1	152*	0	1		
McDonald et al. (1980)[f]	M	9767	10.0	1926-75	20+	3291	3019.3	109	230	184.0	125*	209	203.7	103	10	0		
McDonald et al. (1980)[f]	F	440	7.0	1926-75	20+	84			1	1.2	83				1	0		
Nicholson et. al. (1979)[f,h]	M	544	0.0	1961-77	20+	178	159.9	111	25	11.1	225*	10	9.5	105	1	0		
McDonald et. al. (1984)[e]	M	3177	3.5	1938-77	20+	803	740.1	109	73	49.1	149*	59	51.6	114	0[i]	0		
Rubino et al. (1979)[f]	M	952	2.0	1946-75	20+	220	160.2	137	9	8.7	103	15	14.5	103	1[j]	0		Larynx[k]
Weiss (1977)[e]	M	254	6.1	1945-74		66	108.8	61	4	4.3	93	4	3.8	105	0	0		
Predominantly chrysotile (>98%)																		
McDonald et al. (1983b)[e,l]	M	4137	2.7	1938-77	20+	895	821.1	109	53	50.5	105	54	47.9	113	10	4		
Robinson et al. (1979)[e,l]	M	2722	2.1	1940-75	0	912	741.3	123	49	36.1	136*	50	41.4	121	4	5	4	
Robinson et al. (1979)[e,l]	F	554	3.1	1940-75		128	88.3	145	14	1.7	824*	8	6.0	133	1	1	2	
Mancuso & El-Attar (1967)[e,l]	MF	1493		1940-64		330	139.7	236	33	14.8	223*	16	8.9	180*	1	8		
Peto (1977)[e]	M	822	3.2	1933-74	10+	293	224.9	130	49	22.9	214*	16	15.7	102	9	0		
Thomas et al. (1982)[e,m]	M	1592	3.3	1936-77	15+	261	243.2	107	22	25.8	85	14	14.1	99	2	0		
Amosite																		
Acheson et al. (1984)[e,n]	M	4820	0.5	1947-78		333	298.8	111	57	29.1	196*	19	17.1	111	4	1		
Seidman et al. (1979)[e]	M	820	4.6	1961-76	5+	528	397.2	133	83	21.9	380*	28	22.7	123	7	7		
Predominantly Crocidolite[o]																		
Acheson et al. (1982)[e]	F	757	2.4	1951-80	10+	219	203.5	107	13	6.6	197*	5	4.0	125	3	2		Ovary
Hobbs et al. (1980)[f]	M	6200	20.0	1938-76	15+	526	587.2	90	60	38.2	157*				17	0	14	
Jones et al. (1980)[e,p]	F	951	39.2	1941-78		166			12	6.3	190*	10	20.3	49	13	4		
Wignall & Fox (1982)[e,p]	F	523	6.5	1951-77	10+	133	139.0	96	10	3.7	273*	7	10.7	65	9	3		Ovary
McDonald & McDonald (1978)[e]	MF	199	11.6	1939-75		53			7	2.4[q]	292*				3	6		
Anthophyllite																		
Meurman et al. (1974)[f]	MF	1092	4.7	1936-69		248			21	12.6	167*	7	14.9	47	0	0		
Talc (Tremolite)																		
Kleinfeld et al. (1974)[f]	M	260		1944-69	15+	108			13	4.5	289*	7	6.9	101	0	1		
Brown et al. (1979)[f]	M	398	4.0	1947-75		74	61.3	120	9	3.0	270*	3	3.0	100	0	1[r]		

TABLE 4-1 (Continued)

[n] Amosite was the predominant fiber used. However, chrysotile was also used between 1946 and 1973.
[o] All of the groups in this category had a high exposure to crocidolite. In some cases, however, there was also a substantial exposure to chrysotile.
[p] Two cohorts at the same facility with different definitions and follow-up periods.
[q] Estimated as a proportion of deaths.
[r] May have had exposure to asbestos in the construction industry.
[s] Pleural mesothelioma or lung cancer.
[t] Number of deaths based upon a review of all medical evidence.
[u] No cases observed through the period of follow-up. Three cases have occurred subsequently.
[v] No cases occurred in the cohort as defined during the period of observation. Two occurred in individuals prior to 20 years from onset of employment and nine cases (8 pleural and 1 peritoneal) have developed subsequent to termination of follow-up (Weill 1984).

*p <0.05.

Source: Adapted from EPA 1986

death from mesothelioma appears to be independent of the age at whi exposure occurs. The median time to death due to mesothelioma from exposure was found to be approximately 36 years in a large study of asbestos-exposed insulation workers (Selikoff et al. 1979). However, the increase in risk from mesothelioma with time from onset of exposure appears to lessen after approximately 40 years of exposure, and absolute risk appears to decline after about 50 years of exposure (Nicholson et al. 1982). It has been suggested that this effect may be the result of competing mortality from other asbestos-related diseases, misdiagnosis of disease in older individuals, statistical fluctuations associated with the lower incidences of mesothelioma, or selection processes such as differing exposure patterns. Mesothelioma incidences do not appear to be influenced by an interaction between cigarette smoking and exposure to asbestos.

A number of epidemiological studies have documented significant excess cancer risks at various gastrointestinal sites (EPA 1986). Studies that do not show this relationship generally have methodological problems or are not powerful enough to show a significant effect. The majority of positive studies show an excess of cancer at GI sites that is approximately 10% to 40% of the observed respiratory cancer excess. In addition, kidney and urinary tract cancers were found to be significantly elevated in two large studies (Selikoff et al. 1979, Puntoni et al. 1979), and excess ovarian cancers have been reported among female workers (Newhouse et al. 1972, Wignall and Fox 1982, Acheson et al. 1982).

Epidemiological data suggest that occupational exposure to amphiboles may be associated with a greater risk of mesothelioma than is exposure to chrysotile. The differences in mesothelioma risk are more pronounced for peritoneal than for pleural mesotheliomas. No clear risk differences related to fiber type have been demonstrated for lung cancer (OSHA 1986, EPA 1986). Some of the reported exposure response differences may be related to physical characteristics of different types of asbestos fibers. For example, crocidolite and amosite, which are amphiboles, tend to be long and thin, whereas chrysotile fibers tend to be curly. Long, thin fibers are more likely to reach the lung and lower respiratory system than curly fibers which present

Thomson 1965, Wagner et al. 1960), these studies are not individua convincing because of methodological inadequacies. Studies examin asbestos-related lung cancer among nonoccupationally exposed indiv not been completed.

A number of epidemiological studies have examined the relationship between cancer incidence and the presence of asbestos fibers in drinking water. Municipal water for Duluth, Minnesota, obtained from Lake Superior, reportedly contains high asbestos concentrations related to deposition of mine tailings into the lake. The water supplies of several communities in Connecticut, Utah, and Escambia County, Florida contain elevated levels of asbestos as a result of the deterioration of asbestos-cement (AC) water mains over time. In the San Francisco Bay area and the Puget Sound area, some water supplies contain elevated concentrations of asbestos of natural origin. High concentrations of asbestos due to extensive mining operations have been identified in drinking water in Quebec, Canada. A brief summary of studies conducted in these areas follows.

Among residents of Duluth, Minnesota, elevated risk ratios (Duluth/comparison group) for GI cancers, particularly of the stomach, rectum, and pancreas, have been reported (Mason and McKay 1974, Levy et al. 1976, Sigurdson et al. 1981). However, results for this community have not been consistent over time.

Two epidemiological studies were conducted on relatively small populations in Quebec, Canada exposed to very high concentrations of chrysotile in drinking water. In one of these studies, examination of mortality rates by Wigle (1977) revealed excess incidences of stomach and lung cancer in males and pancreatic cancer in females. However, male mortality was likely to have been from occupational exposure. Although the pancreas has not been directly implicated as a site of excess cancer associated with exposure to asbestos, it should be noted that in some other studies, peritoneal mesotheliomas have been misdiagnosed as pancreatic cancers. In the other study (Toft et al. 1981), the excess stomach and lung cancers observed also were likely to be associated with occupational exposures.

priorities for specific etiologic hypotheses that should be tested to establish risk levels for ingested asbestos.

4.2 NONCARCINOGENIC EFFECTS

Three types of noncarcinogenic effects of asbestos can be identified within the respiratory system: (1) an accumulation of fibers in lung tissue, (2) pleural plaques and thickening, and (3) diffuse pulmonary interstitial fibrosis, which can lead to disabling asbestosis (CPSC 1983). The first two of these three effects are generally considered to be markers of asbestos exposure but are not associated with adverse health effects. The only exception is pleural thickening, which can lead to disabling lung restrictions.

Asbestosis is a chronic disease characterized by breathlessness and impaired lung function and is associated with functional disability and early mortality (CPSC 1983). Asbestosis, as evidenced by irregular opacities in the lung, has been reported in 50-80 percent of individuals in groups with heavy occupational exposures beginning more than 20 years earlier (EPA 1986). It has been noted that in many circumstances, fibrosis progress continued after cessation of exposure.

All types of asbestos are capable of causing asbestosis. Mortality from asbestosis is substantial among occupationally exposed persons, but has not been reported among individuals not occupationally exposed (EPA 1986). This is because development of symptoms characteristic of asbestosis appears to require the fibrotic destruction of a substantial lung volume, which in turn depends on inhalation of quantities of asbestos not typically encountered outside of the occupational setting (CDHS 1986). These and other studies suggest that noncarcinogenic disease is not of importance at exposure levels found in environmental circumstances, and that at such exposures the primary risk consideration should be cancer rather than nonmalignant disease.

5.0 DESCRIPTION OF HEALTH EFFECTS IN EXPERIMENTAL ANIMALS

Experimental animal studies confirm the identification of asbestos-related diseases observed in humans (NRC 1984, EPA 1986). In addition, experimental animal studies provide important information, not available from human studies, on the disposition, clearance, and retention of fibers, as well as cellular changes at short times after exposure (EPA 1986). Unfortunately, one of the most important questions raised by human studies, that of the role of fiber type and size, is only partially answered by animal research (EPA 1986). Injection and implantation studies in animals have shown longer and thinner fibers to be more carcinogenic than shorter ones (EPA 1986). However, the size-dependence of the movement of fibers to mesothelial and other tissues is not fully elucidated, and the questions raised by human studies concerning the relative carcinogenicity of different asbestos varieties still remain (EPA 1986).

Investigators have induced lung tumors, mesothelioma, and fibrosis after administration of asbestos to animals by inhalation or by injection directly into the peritoneum or pleural space (EPA 1986). Results of bioassays in which asbestos was ingested (i.e., directly or via inhalation) are inconclusive (NRC 1984), although in a NTP (1984) bioassay a significant increase in benign epithelial neoplasms in the large intestine was interpreted as limited evidence that orally ingested chrysotile fibers may be carcinogenic (EPA 1985a).

The conclusions that can be drawn from animal bioassays are limited because: (1) in most of the experiments only one dose level was administered, (2) the dose administered was not always adequately characterized (e.g., fiber length and diameter), (3) the doses were expressed on a mass basis, whereas fiber counts would have been more helpful for purposes of quantitative risk assessment, (4) many of the studies suffered from an insufficient number of experimental animals and from an inadequate exposure time to asbestos, (5) studies were not always lifetime studies, (6) survival data were poor or not reported, (7) significant information on experimental protocols was

control mouse had the same tumor type. As in the earlier experiment, information on survival time was not provided. Therefore, it is not clear if a significant number of experimental animals (other than rats) survived to be at risk from late-developing tumors.

Studies by Reeves et al. (1974) also indicate that there are species and strain differences in fibrogenic response. After inhalation of chrysotile, granulomas (distinctive focal lesions formed as the result of an inflammatory reaction) and focal fibrosis have been observed in the rat and guinea pig but not in the mouse. The fibrogenic potential of chrysotile, which had been substantially reduced in length and possibly altered by milling, was much less than that of the amphiboles. Moreover, studies by Lee et al. (1981) showed a direct relationship between dosage of fibers and development of fibrosis in the rat, whereas less prominent changes occurred in the hamster and guinea pig.

Wagner et al. (1974) compared the carcinogenic effect of five different UICC (Union Internationale Contre le Cancer) asbestos samples (i.e., amosite, anthophyllite, crocidolite, Canadian chrysotile, and Rhodesian chrysotile). Wistar SPF rats were exposed to the five UICC asbestos fiber samples at concentrations from 10.1 to 14.7 mg/m^3 for the different fiber types. Exposure was 7 hours/day, 5 day/week for 1 day or 3, 6, 12, or 24 months. All of the animals were followed for lifetime. Survival times were not significantly affected by exposure. All fiber types induced adenocarcinoma and squamous cell carcinoma in the lung. Incidences were 11/146, 16/145, 16/141, 17/137, and 30/144, for the respective fiber types. Mesotheliomas were also induced. No tumors were found in control animals. In general, tumor incidence increased with length of exposure. The development of asbestosis, was also documented. However, it was found that animals with lung tumors had no evidence of asbestosis, or they had a minimal or slight case of asbestosis. Wagner et al. (1977) also compared the effects of inhalation of a superfine chrysotile to the effects of inhalation of a pure nonfibrous talc. One adenocarcinoma was found in 24 CO Wistar rats exposed to 10.8 mg/m^3 chrysotile for 37.5 hours per week for 12 months and observed for 24 months. No tumors were found in control animals exposed to nonfibrous talc.

providing limited evidence that ingested chrysotile asbestos fibers may be carcinogenic.

The results of a series of feeding experiments with different sources of chrysotile and crocidolite were reported by Gross et al. (1974). This paper incorporated data from unpublished results of various studies conducted by three laboratories. Animals fed asbestos by gavage in butter or margarine for up to 21 months failed to provide evidence of a carcinogenic effect. The experiments were flawed for the following reasons: The number or rats in the experimental groups was small, the doses of asbestos were limited, significant information on experimental protocol was missing, and systemic histological examination was not performed on a significant number of rats (Condie 1983). Furthermore, differences in the sample handling and analytical techniques associated with characterizing a solid matrix in terms of potential exposure may not have been adequately considered. Gibel et al. (1976) reported an increase in malignant tumors of the lung, kidney, liver, and reticuloendothelial system in rats fed asbestos filter material containing chrysotile. The control group had a similar incidence of liver tumors. There was no increase in intestinal tumors in either the control or treatment group. Filter material containing chrysotile was administered at 20 mg/day for lifetime. The filter material was composed of sulfated cellulose, a condensation resin, and chrysotile asbestos (53%). No information was provided regarding the size and shape of the asbestos fibers that were incorporated in the filter material. The authors stated that no conclusions could be made from their test results regarding the pathogenesis of the tumors caused by the oral intake of asbestos material. The relationship of this study to asbestos carcinogenicity was also confounded by the presence of several substances in the filter material, which were not clearly identified (Condie 1983).

Donham et al. (1980) reported equivocal results in a lifetime rat feeding study using a diet containing 10% chrysotile. Because of the high level of asbestos in the feed, a nonnutritive cellulose fiber control group was included. In this study, only the colon and rectum were examined microscopically. Three colon tumors were found in both treated and control groups. One mesothelioma was found in the treated group. There was evidence of penetration of asbestos

of C-cell carcinomas of the thyroid and monocytic leukemia. None of these tumors were considered treatment related.

In the NTP (1984) bioassay, male rats ingesting intermediate range chrysotile fibers at 1% in the diet for lifetime, starting with the dams of the test animals, had a significant increase in benign epithelial neoplasms in the large intestine. This was interpreted as limited evidence that ingested chrysotile asbestos fibers may be carcinogenic (EPA 1985a).

6.0 DOSE-RESPONSE ASSESSMENT

When based on human data, risk assessments are typically derived from studies of human populations in which it is not possible to pre-select the participants, accurately establish the levels of exposure, or control for outside factors (e.g., presence of other contaminants). When based on animal bioassays, such assessments are typically derived from high dose, short-term exposure studies, not the low dose, long-term exposures from which criteria are set. Risk assessment thus frequently requires extrapolation between different routes of administration, extrapolation from animal to human effects, and extrapolation from test groups to the population at large. Despite such uncertainties, risk assessment can provide a quantitative estimate of health risks to the general population and permit the establishment of standards or action levels for controlling exposure.

There is general agreement on dose-response models for lung cancer and mesothelioma in a number of published quantitative risk assessments for nonoccupational or low-level exposures to asbestos, and similar risk estimates were generally related to selection of the specific studies considered in each risk assessment. It should be noted that some investigators (ORC 1984, ACA 1979a) calculated risk estimates using data from individual occupational studies and presented the results as a range of the individual results obtained. Other investigators (EPA 1986, CDHS 1986, CPSC 1983, NRC 1984), however, estimated risks at lower exposure levels by using average risk estimates based on a number of epidemiological studies of asbestos-exposed workers. This approach was used, in part, because of the great uncertainty regarding the identity, physical structure, and other characteristics of asbestos in both occupational settings and unstudied nonoccupational settings.

6.1 INHALATION

EPA (1986), in the Airborne Asbestos Health Assessment Update, described developments in studies of asbestos-related health effects since 1972. In

I_L (a,y,t,d,f) = lung cancer incidence observed or projected in a population of age a, observed in calendar period y, at t years from onset of asbestos exposure, and at average exposure intensity f;

I_E (a,y) = age- and calendar period-specific lung cancer incidence expected in the absence of exposure;

K_L = carcinogenic potency expressed as the fractional increase in lung cancer risk per unit of cumulative exposure in fiber-year/milliliter (f-y/ml);

f = intensity of exposure to all asbestos fibers longer than 5 microns (f/ml) as measured by optical microscopy; and

d = duration of exposure up to 10 years from observation of cancer (t, the time from onset of asbestos exposure, minus 10 years to allow for a minimum latency period).

According to this model, excess risk of lung cancer from asbestos exposure is proportional to the cumulative exposure (duration x intensity) and the underlying risk in the absence of exposure (e.g., smoking strongly influences the underlying risk). The time course of lung cancer is determined primarily by the time course of the underlying risk. If smoking data are available, I_L and I_E can be smoking-specific incidences.

Because mesothelioma is very rare in the general population, an absolute risk model is most appropriate for quantifying the dose-response relationship. Using an absolute risk model for mesothelioma and a linear dose-response relationship with no threshold, the incidence of mesothelioma for varying times of exposure can be expressed (EPA 1986) as

$$I_M(t,d,f) = K_M \times f\,[(T-10)^3 - (T-10-d)^3] \quad \text{for } T > 10+d$$

$$= K_M \times f\,(T-10)^3 \quad \text{for } 10+d > T > 10$$

$$= 0 \quad \text{for } 10 > T$$

where

I_M (t,d,f) = mesothelioma incidence at t years from onset of exposure, for duration d, at concentration f;

K_M = carcinogenic potency expressed as the incidence of mesothelioma per unit of exposure in f-y^3/ml;

Four epidemiological studies provided quantitative data suitable for calculation of potency factors for mesothelioma (K_M, the incidence per f-y^3/ml exposure), and a number of other studies provided corroborative but less precise quantitative data. These studies also considered exposure to amphibole asbestos, to chrysotile asbestos, and to mixtures of asbestos fiber types. The ratios of a measure of mesothelioma risk to excess lung cancer risk were found to be approximately equal for these studies, suggesting that the same factors that affect K_L also affect K_M. However, other studies suggest that K_M may be greater among groups exposed to substantial quantities of crocidolite than among groups exposed to other fiber types. In addition, the risk of peritoneal mesothelioma appears to be lower from exposure to chrysotile than from exposure to either crocidolite or amosite, although misdiagnosis of the disease may be an important consideration. Finally, incidence rates for mesothelioma increase more rapidly with time from first exposure than those for lung cancer. Early exposures are therefore most important in determining lifetime risks, although effects are mostly expected later in life. After consideration of these and other factors, EPA (1986) calculated an average value for K_M of 1.0×10^{-8} $(f\text{-}y^3/ml)^{-1}$ from the available epidemiological studies as the best estimate for environmental exposures. Although it was not possible to determine directly the 95% confidence limits on K_M, a multiplicative factor of 5 was estimated for the average value of K_M, and a multiplicative factor of 20 was estimated for its application to any unstudied exposure circumstance.

Using a relative risk model for lung cancer and an absolute risk model for mesothelioma with the appropriate potency factors (K_L and K_M), EPA (1986) calculated best estimates of risks resulting from continuous exposures to 0.0001 or 0.01 f/ml asbestos. The values for continuous exposure were derived by multiplying risks obtained from occupational exposure data by 4.2, the ratio of total hours in a week to 40 hours. The value of 0.0001 f/ml is typical of urban ambient air and is equivalent to about 3 ng/m^3. The value of 0.01 f/ml (300 ng/m^3) has been measured in several environmental exposure circumstances. Measurements of environmental exposure to asbestos are summarized in the Airborne Health Assessment update prepared by EPA (1986).

An alternative method of calculating risk uses the unit risk conc
(1987a,b) used the information from EPA (1986) to calculate a unit ri...
will yield the excess cancer risk when multiplied by ambient concentrations. EPA (1987a,b) assumed that risks of mesothelioma and lung cancer were additive, that the population was 51% female and 49% male, that occupational exposure could be converted to environmental exposure using ratios of worker-to-general-population breathing rates, and that a conversion factor of 30 $\mu g/m^3$ = 1 f/ml was acceptable. This yielded a unit risk of 2.3186×10^{-1} $(f/ml)^{-1}$ for continuous lifetime exposure.

6.2 INGESTION

The scientific literature on health effects resulting from asbestos ingestion is not as well developed as that for asbestos inhalation. Very few studies were found in the available literature that investigated toxic, noncancer effects following ingestion of asbestos fibers (EPA 1985a). Studies of whether increased cancer incidence occurs due to direct asbestos ingestion include animal ingestion studies and epidemiological studies of ingestion of asbestos in drinking water. In addition, some inhalation studies have considered the ingestion of asbestos as a secondary route of exposure following inhalation. Given the lack of conclusive evidence in ingestion studies and the possible link between inhalation and ingestion, a risk assessment for asbestos ingestion must consider all available alternatives. Such a risk assessment could be based on human ingestion studies, animal ingestion studies, human studies of ingestion via inhalation, and animal studies of ingestion via inhalation.

6.2.1 HUMAN INGESTION STUDIES

Methodological weaknesses and limitations found in epidemiological studies of asbestos ingestion in drinking water lead to the conclusion that no individual study or aggregation of studies exists that would establish risk levels from ingested asbestos in drinking water (Marsh 1983). The most serious deficiency in the California Bay study which found a possible association between asbestos in drinking water and cancer incidence (Conforti 1983) was the substantial problems in classifying exposure because population data rather than individual

6.2.3 HUMAN STUDIES OF INGESTION VIA INHALATION

Human studies of workers exposed to airborne asbestos unequivocally demonstrate an excess of gastrointestinal cancer in some of the groups surveyed (EPA 1980). A likely route of exposure to the gastrointestinal tract from such exposures is from the fibers cleared from the lung and bronchial tract and subsequently swallowed (EPA 1980). Using information on airborne exposures to workers, it is possible to estimate an approximate exposure level to the gastrointestinal tract from estimates of airborne asbestos concentrations.

Two organizations (EPA 1980, NRC 1983b) have based risk estimates for asbestos ingestion on human inhalation studies. Both studies were reviewed recently (EPA 1985a) as part of the EPA development of drinking water criteria for asbestos. The use of human inhalation studies for risk assessment is appropriate because they provided sufficient scientific evidence in comparison with the limited evidence found in direct ingestion studies. Section 7.2.5 "Risk Assessment" will summarize the NRC (1983b) analysis as the recommended model for estimation of human risk associated with asbestos ingestion.

6.2.4 ANIMAL STUDIES OF INGESTION VIA INHALATION

Since some evidence is presented in human inhalation studies for a correlation between asbestos inhalation and increased GI tract cancer incidence, it is reasonable to evaluate the usefulness of animal inhalation studies in conducting a risk assessment for asbestos ingestion. Arguments for the use of such studies are that (1) they provide another method of risk analysis and source of risk estimates, (2) they allow calculation of risk while eliminating many of the uncertainties inherent in epidemiological studies, and (3) they allow evaluation of the validity of animal-to-human risk extrapolations. Given the absence of significant carcinogenic effects in the GI tract following inhalation of asbestos by animals and the availability of human inhalation data, animal inhalation studies will not be utilized in the risk assessment for asbestos ingestion.

A linear dose-effect relationship for lung cancer and exposure to asbestos was most clearly shown by results reported by Henderson and Enterline (1979). For GI cancers, few data have been published to establish or refute linearity, even at high doses. There is a theoretical argument (Crump et al. 1976) that suggests that cancer incidence should vary approximately linearly with dose for low doses particularly when there is an appreciable background of carcinogenicity in unexposed populations. In this case, the assumption of a linear relationship between GI cancer and low dose exposure to asbestos appears reasonable.

Step 2. Conversion of Inhaled Dose to Ingested Dose

Since the excess GI cancers in the workers are assumed to be caused by the asbestos fibers that these workers swallowed rather than inhaled, the dose calculated in Step 1 must be converted to fibers swallowed. NRC estimated that:

Breathing 1 fiber/ml for 1 year = 588×10^6 fibers swallowed/year

where

588×10^6 fibers swallowed/year = 1 fiber breathed/ml x 10^6 ml/m^3 (a)(b)(c)(d);

a = 8 m^3 air breathed/day worked;

b = 5 days worked/week;

c = 49 weeks worked/year; and

d = 0.3 fibers swallowed/1 fiber breathed.

The value of 0.3 fibers swallowed/1 fiber breathed is based on animal studies (Morgan et al. 1975) and estimated for humans (Dement 1979). The EPA risk assessment to derive ambient water quality criteria (EPA 1980) used a ratio of 1.0. Although EPA recognized that this may be an overestimate, EPA concluded that this may be partly offset by fibers that are swallowed directly. The factor used by NRC, which does not allow for directly ingested asbestos, is more closely tied to current scientific data.

fibers/liters for risk level of 10^{-7}, 11,000 TEM fibers/liter for risk level of 10^{-6}, and 110,000 TEM fibers/liter for risk level of 10^{-5}.

In order to evaluate the 1985 EPA risk assessment used to derive a proposed drinking water MCLG, the steps leading to establishment of cancer risk levels will be presented.

Step 1. Establishment of Animal Fiber Dose

A key assumption was that asbestos in dry diet would have the same effect as asbestos in water. To establish the daily dose

(0.38 kg x 0.05)(10,000 mg/kg of diet) = 190 mg/day (or 500 mg/kg/day)

where

0.38 kg = weight of male rat;

0.05 = rat consumes 5% of body weight/day; and

10,000 mg/kg = fibers make up 1% of diet.

In order to convert from a daily mass dose to a daily fiber dose, the following conversion was used:

$$500 \text{ mg/kg/day} \times 0.129 \times 10^{9} \text{ f/mg} = 6.45 \times 10^{10} \text{ f/kg/day}$$

where the conversion factor 0.129×10^{-9} f/mg is based on TEM measurements performed at the Illinois Institute of Technology Research Institute (NTP 1984).

Step 2. Establishment of Equivalent Human Dose

In order to determine the human equivalent dose, the EPA procedure has been to assume dosage equivalency on a dose/(body weight)$^{2/3}$ basis. The equivalent human dosage for a 70-kg human is

$(6.45 \times 10^{10}$ f/kg bw rat/day$)(70/0.380)^{-1/3} = 1.13 \times 10^{10}$ f/kg bw human/day.

TABLE 6-1

CALCULATED LIFETIME RISKS PER 100,000 PERSONS OF DEATH FROM MESOTHELIOMA AND LUNG CANCER FROM CONTINUOUS ASBESTOS EXPOSURES[a]

Age at Onset of Exposure	Concentration = 0.0001 f/ml Years of Exposure					Concentration = 0.01 f/ml Years of Exposure				
	1	5	10	20	Life-time	1	5	10	20	Life-time
Mesothelioma in Females										
0	0.1	0.7	1.2	2.0	2.8	14.6	67.1	120.8	196.0	275.2
10	0.1	0.4	0.8	1.2	1.5	9.4	42.6	75.5	118.7	152.5
20	0.1	0.3	0.4	0.7	0.8	5.6	25.1	43.5	65.7	78.8
30	0.0	0.1	0.2	0.3	0.4	3.1	13.3	22.4	31.9	35.7
50	0.0	0.0	0.0	0.0	0.0	0.6	2.1	3.2	3.9	3.9
Lung Cancer in Females[b]										
0	0.0	0.0	0.1	0.2	0.5	1.0	4.6	9.2	18.5	52.5
10	0.0	0.0	0.1	0.2	0.4	1.0	4.6	9.2	18.6	43.4
20	0.0	0.0	0.1	0.2	0.3	1.0	4.6	9.2	18.2	34.3
30	0.0	0.0	0.1	0.2	0.3	1.0	4.6	9.0	16.7	25.1
50	0.0	0.0	0.1	0.1	0.1	0.7	3.1	5.5	8.1	8.8
Mesothelioma in Males										
0	0.1	0.5	0.9	1.5	1.9	11.2	51.0	91.1	145.7	192.8
10	0.1	0.3	0.6	0.8	1.1	7.0	31.2	58.2	84.7	106.8
20	0.0	0.2	0.3	0.4	0.5	4.1	17.5	30.1	44.5	51.7
30	0.0	0.1	0.1	0.2	0.2	2.1	8.8	14.6	20.4	22.3
50	0.0	0.0	0.0	0.0	0.0	0.3	1.1	1.8	2.0	2.1
Lung Cancer in Males[b]										
0	0.0	0.1	0.3	0.6	1.7	2.9	14.8	29.7	59.2	170.5
10	0.0	0.1	0.3	0.6	1.4	2.9	14.9	29.8	59.5	142.0
20	0.0	0.2	0.3	0.6	1.1	3.1	15.0	30.0	59.4	113.0
30	0.0	0.1	0.3	0.6	0.8	3.1	14.9	29.8	56.6	84.8
50	0.0	0.1	0.2	0.3	0.3	2.5	11.5	20.3	29.1	30.2

[a]The 95% upper confidence limit on the risk values for lung cancer for an unstudied exposure circumstance is about 10 times the tabulated values. The 95% upper confidence limit on the risk values for mesothelioma for an unstudied exposure circumstance is about 20 times the tabulated values.

[b]Mortality rates for smokers and nonsmokers differ. General population risks are shown, calculated for a population in which 67% of males and 33% of females smoke.

Source: EPA 1986

7.0 SUMMARY OF CRITERIA

Recommended criteria for exposure to asbestos by ingestion or inhalation are summarized in Table 7-1. These criteria are discussed in detail in Section 6.0, "Dose-Response Assessment." A number of other criteria for protection of individuals exposed in the workplace or in environmental settings have also been recommended by government agencies and other advisory groups. These criteria are presented for comparison in Table 7-2.

The criteria for exposure by inhalation to asbestos in ambient air shown in Table 7-1 are expressed in terms of PCM fibers per ml (i.e., fibers >5 microns in length, aspect ratio >3.1). These limitations are required primarily because the majority of available studies on which the criteria are based employed PCM analytical techniques. Thus, individual asbestos minerals could not be distinguished and were not considered separately. Further, although it appears that longer, thinner asbestos fibers have greater biological activity than shorter thicker fibers, the relative potency of different asbestos size factions has not been adequately characterized.

Because TEM is currently the accepted and well-established procedure for measuring asbestos in ambient air, consideration must be given to appropriate conversion factors. Asbestos counts, even when limited to the fraction greater than 5 microns, differ widely between PCM and TEM. One approach for conversion would be to count only those TEM fibers larger than 5 microns with aspect ratios greater than 3.1 but with a minimum diameter of 0.2 microns as well. Thus, a "PCM equivalent" fraction is generated. Another accepted approach is a two-step process beginning with converting fiber counts to mass per unit volume by the established procedure (Chatfield, 1983). Data from earlier studies are available to convert optical fiber counts (such as the inhalation criteria presented in the table) to mass concentrations as well. A value of 30 micrograms/m^3 per PCM f/ml is recommended and represents the geometric means of a range of literature derived conversion factors (see Chapter 3). Although a high degree of uncertainty is associated with this approach, it has the advantage of indirectly considering, to some extent, the contribution of

Where is the evidence of populations exposed to the level of asbestos in water

TABLE 7-2

SUMMARY OF ADDITIONAL ASBESTOS CRITERIA

OSHA Standard

What level of CA pop. is exposed to the level from Hensuke site in the drinking water supply parameter by EPA?

PEL of a 0.2 f/cc as an 8-hour TWA

NIOSH Recommended Standards:

0.1 f/ml as an 8-hour TWA
0.5 f/ml as a 15-minute ceiling level

ACGIH Threshold Limit Value

Amosite, 0.5 fibers greater than 5 microns in length/ml
Chrysotile, 2 fibers greater than 5 microns in length/ml
Crocidolite, 0.2 fibers greater than 5 microns in length/ml
Other forms, 2 fibers greater than 5 microns in length/ml

Office of Air Quality Planning and Standards (EPA 1987a,b)

Risk	Concentrations
10^{-5}	4.3×10^{-5} fibers/ml
10^{-6}	4.3×10^{-6} fibers/ml
10^{-7}	4.3×10^{-7} fibers/ml

Ambient Water Quality Criteria (EPA 1980)

Risk	Concentrations
10^{-5}	300,000 fibers/liter
10^{-6}	30,000 fibers/liter
10^{-7}	3,000 fibers/liter

Drinking Water Criteria Draft

Risk	Concentrations	
	Best Estimate Values	95% Lower Limits
10^{-5}	1.3×10^{8} fibers/liter	7.1×10^{7}
10^{-6}	1.3×10^{7} fibers/liter	7.1×10^{6}
10^{-7}	1.3×10^{6} fibers/liter	7.1×10^{5}

Proposed Drinking Water MCLG is 7.1×10^{6} fibers/liter associated with a 1×10^{-6} risk. This criterion is limited to fibers > 10 microns in length.

are not based strictly on health considerations alone but take other factors into account as well.

The ambient water quality criteria developed by the EPA are derived from data on the increased incidence of peritoneal mesothelioma and GI tract cancer in humans exposed occupationally to asbestos. The derivation assumes that much or all of this increased disease incidence is caused by fibers ingested following clearance from the respiratory tract. The asbestos concentrations indicated in Table 7-2 are expressed as total fibers counted using electron microscopy analysis. The excess cancer risks associated with ingestion of 2 liters of water per day for a 70-year lifetime containing asbestos at the indicated concentrations are shown. The Drinking Water Draft criteria and Proposed Drinking Water MCLG shown in Table 7-2 are calculated from animal ingestion studies which considered the association between fiber length and carcinogenicity. The criteria are based on measurement of fibers >10 microns in length using electron microscopy techniques.

8.0 ECOTOXICITY

In this section, the fate and transport of asbestos fibers in [illegible] as well as the toxic effects of asbestos fibers on aquatic life are presented. Only toxicity to aquatic life is considered; no data are available on the effects of asbestos on terrestrial wildlife although the results of rodent bioassays (Section 5.0) may be relevant for evaluation of terrestrial species. In addition, dose-response data are inadequate to recommend specific criteria for the protection of aquatic life.

8.1 FATE AND TRANSPORT

Asbestos fibers have very limited chemical reactivity but are susceptible to physical breakup into smaller and/or thinner fibers. Although the fibers are not soluble in water, cations may be leached from them leaving the silica structure behind (Choi and Smith 1972). The effect that leaching of cations has on the structural integrity of the crystal is unclear (EPA 1979). Acid leaching alters surface properties of chrysotile, but not of amphibole asbestos fibers (Seshan 1983).

Asbestos fibers from environmental samples obtained in California were found to be smaller in length and width than freshly mined fibers or fibers present in industrial applications (Bales et al. 1984). For example, in raw river water, fiber sizes ranged between 0.05-0.1 microns in width and 0.5-1.0 microns in length. Incorporating data concerning fiber size, density, and surface charge, Bales et al. (1984) modeled concentrations of chrysotile asbestos originating from naturally weathering rock in California water systems. Asbestos fiber concentrations in surface water were reduced by a factor of 10 as a result of passage through reservoirs with a retention time of 1 year. Reservoirs with a retention time of 3 years reduced asbestos concentrations by a factor of 1,000. The authors (Bales et al. 1984) attributed the reduction to coagulation and settling. In the same study, it was found that 86%-99.8% of asbestos fibers were removed by water treatment facilities that utilized coagulation and filtration methods. Amphibole fiber concentrations in Lake Superior resulting from mining activity in the western end of the lake are reduced by more than

differences between fiber concentrations in both liver and kidney tissues but not in muscle tissues of fish from contaminated and clean areas. Laboratory exposure of fish did not result in large differences in tissue concentrations, which suggests that an unidentified exposure mechanism may be operating in the field. Batterman and Cook (1981) also observed a difference in fiber size in field- versus laboratory-exposed fish which may be related to differences in tissue uptake between laboratory and field. In this regard, Lauth and Schurr (1984) reported the presence of smaller fibers in alga cells than in the water from which they were taken.

Except for leaching in body fluid and stomach acid, biotransformation of asbestos fibers has not been observed.

8.2 AQUATIC TOXICITY

Asbestos fibers are acutely toxic only at very high concentrations. Larval Asiatic clams (Corbicula sp.) had significantly higher mortality rates than controls when exposed to chrysotile fiber concentrations between 10^2-10^8 f/liter. Fathead minnows exposed to 10^{12} f/liter for 96 hours or 10^8 f/liter for 30 days did not exhibit increased mortality over controls (Belanger 1986). Japanese medaka (pisces, Oryzias latipes) exposed to 10^{10} f/liter for 60 days experienced 100% mortality. Stewart and Schurr (1980) reported that maximum mortality of Artemia occurred between 10^7-10^8 f/liter.

Asbestos exposure can result in deleterious impacts on growth, reproduction, physiological equilibrium, and behavioral traits in algae. Exposure to chrysotile fibers at 1-1.5x10^6 f/liter for 48 hours resulted in severe clumping of cells of the algae Cryptamonas erosa (Lauth and Schurr 1983). It was postulated that this would result in loss of mobility and death due to settling out.

Adult and juvenile Asiatic clams exhibited reduced siphoning rate and shell growth when exposed to 10^5 f/liter for 30 days (Belanger 1986). Juvenile clams also had reduced weight gain at 10^4 f/liter in summer temperatures, and at 10^5 f/liter in winter temperatures. Weight gain of juvenile fathead minnows

The conclusions of the EPA Ambient Water Quality Criteria Document (EPA 1980) are that no statements concerning the acute or chronic toxicity of asbestos in freshwater or saltwater organisms can be made.

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Appendix D
Analytical Data and QA/QC Evaluation Results

APPENDIX D

This appendix presents a summary of analytic data generated as a result of field sampling and analysis programs conducted for the remedial investigation. The data presented include the complete results of the surface water, soil, and air sampling and field erosion testing programs conducted by WCC in 1986 and 1987. The summary also present the results of the Quality Assurance/Quality Control (QA/QC) review of the subject data. The QA/QC review was conducted by the EPA or its designated contractor.

The relative validity of the analytic data as determined by the QA/QC review is indicated in the summary on a per-sample basis by the use of particular symbols. These symbols and their explanations are:

- J - Result is estimated and is considered usable for limited purposes only.
- R - Result is rejected and is considered invalid for all purposes.
- U - Parameter was determined but not detected above the listed concentration.
- UJ - Detection limit is estimated and considered usable for limited purposes due to blank contamination or analytical deficiencies.
- NA - Not analyzed.
- () - Result in brackets indicates result is greater than or equal to the instrument detection limit obtained by the laboratory for clean water but less than the contract-required detection limit.

Analytic data not accompanied by a QA/QC review symbol are considered valid for all purposes. The results of the QA/QC review were duly noted and utilized when reporting and interpreting data during all phases of the remedial investigation.