2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO ASBESTOS IN THE UNITED STATES

Asbestos is a generic term for a group of six naturally-occurring, fibrous silicate minerals that have been widely used in commercial products. These minerals are more commonly found in nonfibrous forms that are not asbestos. Asbestos minerals fall into two groups or classes, serpentine asbestos and amphibole asbestos. Chrysotile, a serpentine asbestos, possesses relatively long and flexible crystalline fibers that are capable of being woven. Amphibole asbestos has crystalline fibers that are substantially more brittle than serpentine asbestos. Amphibole asbestos includes amosite, crocidolite, and fibrous forms of tremolite, anthophyllite, and actinolite (see Chapter 4 and Appendix F for more information on chemical and physical properties of asbestos). Over 99% of asbestos used in the United States is chrysotile. As a result of its low cost and desirable properties such as heat and fire resistance, wear and friction characteristics, tensile strength, heat, electrical and sound insulation, adsorption capacity, and resistance to chemical and biological attack, asbestos has been used in a very large number of applications and types of products. In most of its applications, asbestos is bonded with other materials such as Portland cement, plastics, and resins. In other applications, asbestos is used as a loose fibrous mixture or woven as a textile. Use of asbestos in the United States has been declining for 2 decades largely due to health concerns. In 1997, asbestos consumption was 6% of what it was in 1980. The 1997 domestic consumption pattern was 48% for roofing products, 29% for friction products (automobile clutch, brake, and transmission components), and 17% for packing and gaskets (see Chapter 5 for more information on production, import, use, and disposal of asbestos).

Asbestos fibers are chemically inert—they do not evaporate, dissolve, burn, or undergo significant reactions with most chemicals. They do not undergo significant degradation in the environment. Although asbestos is not volatile, small fibers and clumps of fibers may be released to air as dust. Asbestos occurring in natural mineral deposits may be released to the atmosphere when these deposits are disturbed—as in mining operations or during building and construction (see Appendix F for information on occurrence of asbestos in other mineral deposits). Asbestos fibers may also be released during the processing of asbestos minerals and the manufacture, application, use, demolition, and disposal of asbestos-containing products. Asbestos released into the atmosphere will be transported by wind and settle on the ground. Small fibers may remain suspended for long periods of time and be transported long

distances. Asbestos may be released into surface water by erosion and runoff, transported in water, and deposited in the sediment.

Numerous measurements have been performed to determine the concentration of asbestos fibers in environmental media, primarily air. These studies have reported results in a variety of units, including PCM f/mL (fibers per mL air=fibers per cm^3, measured by phase contrast microscopy) and TEM f/mL (fibers measured by transmission electron microscopy) (see Section 3.2.1 and Chapter 6 for additional information regarding exposure and exposure units). Definition of a fiber is critical in these methods. The most widely used definition of a fiber among health professionals is a particle that has a length $5 µm and a length/width ratio of $3:1. Although numerous exposure and health effects studies have employed the PCM method for analysis of airborne asbestos concentrations, the method is not capable of detecting fibers smaller in diameter than approximately 0.2–0.3 µm and these thinner fibers may pose a significant health threat (see Chapter 3 for additional information on the relationships between fiber size and health risk). The PCM method is also incapable of distinguishing between asbestos fiber types or between asbestos and nonasbestos fibers. TEM can be used to detect fibers with diameters as small as 0.01 µm and distinguish between asbestos and nonasbestos fibers, as well as fiber types. Although TEM is the preferred method for measuring air concentrations of asbestos, epidemiological studies of occupational exposure to relatively high levels of asbestos, such as those experienced prior to the institution of recent occupational exposure limits (currently 0.1 f/mL), employed PCM or midget impinger particle counting. Particle counting yielded measurements of mass of particles per volume of air. Reported health effects have predominantly been expressed in terms of PCM concentrations (see Section 3.2.1 for a discussion of the uncertainties in converting from midget impinger particle mass per volume to PCM f/mL). Therefore, comparisons between environmental exposure data and occupational exposures associated with adverse health effects can be most readily made using measurements expressed in terms of PCM.

Inhalation is the primary route by which the general population might be exposed to asbestos. Small quantities of asbestos fibers are ubiquitous in air, arising from natural sources (weathering of asbestos-containing minerals), from windblown soil from hazardous waste sites, deterioration of automobile clutches and brakes, or breakdown of asbestos-containing materials such as insulation (mainly chrysotile). The results of numerous measurements indicate that average concentrations of asbestos in ambient outdoor air are within the range of 10^{-8}– 10^{-4} PCM f/mL; levels in urban areas may be an order of magnitude higher than those in rural areas. Even higher concentrations (up to 0.4 f/mL) have been measured in ambient air surrounding Taiwanese factories that manufacture asbestos-containing products.

Indoor air concentrations of asbestos ranged from approximately 10^{-5} to 10^{-4} f/mL in a study of air concentrations measured in a total of 315 U.S. public and commercial facilities. See Chapter 6 and Appendix F for more detailed information regarding concentrations of asbestos in environmental media.

2.2 SUMMARY OF HEALTH EFFECTS

Epidemiological studies of asbestos-exposed workers and supporting animal studies indicate that inhalation of asbestos is the principal route of exposure of public health concern. Some epidemiological studies have also indicated that oral exposure may be linked to the development of gastrointestinal cancer. Depending largely on size and shape, deposition of inhaled asbestos fibers may occur in lung tissue. Some fibers may be removed by mucociliary clearance or macrophages while others may be retained in the lungs for extended periods. Inhalation exposure is, therefore, generally regarded as cumulative, and exposures have been expressed in terms of concentration of fibers over time or PCM fiber-years/mL (f-yr/mL). Studies in humans and animals indicate that inhalation exposure to asbestos fibers may lead to the development of pulmonary disease including asbestosis and/or lung cancer and mesothelioma of the pleura or peritoneum (see Chapter 2 and Appendix F for more detailed information on evidence for these health effects). In general, noncancer effects in other tissues have not been detected; however, the development of cancer in other tissues (e.g., gastrointestinal tissues) in some worker populations may be related to asbestos exposure. Asbestos-related lung diseases (malignant and nonmalignant) or signs of these diseases have been reported in groups of occupationally exposed humans with cumulative exposures ranging from about 5 to 1,200 f-yr/mL. Such cumulative exposures would result from 40 years of occupational exposure to concentrations ranging from 0.125 to 30 f/mL. Currently, U.S. OSHA regulations require that workplace air concentrations of asbestos not exceed 0.1 f/mL. Although asbestos-related effects have been primarily reported after chronic exposures to asbestos in an occupational setting, these effects have also been described following relatively brief occupational exposures. Exposures of this magnitude are usually not encountered by the general public.

Cancer. There is no doubt that inhalation of asbestos can lead to increased risk of lung cancer and mesothelioma. This has been conclusively demonstrated in numerous studies of occupationally exposed workers, and has been confirmed in a number of animal experiments. For lung cancer, the magnitude of the risk appears to be a complex function of a number of parameters, the most important of which are: (1) the level and the duration of exposure; (2) the time since exposure occurred; (3) the age at which exposure occurred; (4) the tobacco-smoking history of the exposed person; and (5) the type and size distribution of the asbestos fibers.

The last parameter is of special practical importance, since the variability in potency among fibers means that cancer risk from asbestos exposure may vary widely from location to location. Some of this variation may be attributable to differences between the mineral types, but fiber size (length and thickness) appear to be of prime importance. There is strong evidence from animal inhalation studies, intrathoracic and intraperitoneal dosing studies, and *in vitro* studies that long fibers are more carcinogenic than short fibers. However, this should not be construed to mean that shorter fibers are totally without carcinogenic potency. The relation between fiber size and carcinogenicity may vary between lung cancer and mesothelioma, but this is not yet clear.

There is some evidence from animal studies that asbestos-induced lung cancer stems from regions in the lung with advanced fibrosis (asbestosis); however, lung cancer with chrysotile was also produced at fiber concentrations that did not lead to detectable fibrosis.

Because of the large number of variables, it is difficult to make reliable predictions of the magnitude of the cancer risk that may result from exposures of the general population to asbestos levels that are likely to be encountered outside the workplace. Although there is considerable uncertainty in the estimates, EPA calculated, using a linear, no-threshold model, that lifetime exposure to asbestos dust containing 0.0001 fibers >5 μm in length per mL of air could result in about 2–4 excess cancer deaths (lung cancer plus mesothelioma) per 100,000 people. In 2001, EPA has been in the process of reviewing its cancer risk estimates for asbestos.

While lung cancer and mesothelioma are generally associated with chronic exposure to asbestos, there are several studies that indicate that short-term exposures are also of concern. For example, it has been noted that workers exposed to asbestos for only 1–12 months had an increased risk of developing lung cancer a number of years later. In animals, mesotheliomas developed in two rats exposed to high concentrations of amosite or crocidolite for only 1 day. These data are not extensive enough to define the dose- or time-dependency of health risks from short-term exposure to asbestos, but the data do indicate that short-term exposures should not be disregarded.

Asbestos exposure is also suspected of increasing the risk of cancer in the gastrointestinal tract, although the evidence is less consistent than for lung cancer or mesothelioma. Data supporting this view have been derived mainly from three types of studies. First, some studies of workers exposed to asbestos by inhalation have noted small excesses in death rates from gastrointestinal cancer. This is presumed to be due to the transfer of inhaled fibers from the lung to the gastrointestinal tract. Second, some studies

suggest that populations with high levels of asbestos fibers in drinking water may have increased risk of gastrointestinal cancers. Third, one lifetime feeding study in rats indicated that intermediate-length chrysotile can increase the frequency of benign intestinal tumors in male rats. There are several findings, however, that do not support the association. The excess gastrointestinal mortalities noted in workers and in populations exposed through drinking water were usually quite small (from an epidemiological point of view), the follow-up period was of insufficient duration, and consistent results were not found across studies. Also, it is very difficult to determine whether the excesses are due to asbestos or to other factors (exposure to other chemicals, misdiagnosis, dietary factors, alcohol intake, etc.). With regard to the one positive tumorigenicity finding in animals, this must be balanced against the fact that the tumors were both infrequent and benign, and that no significant excess of gastrointestinal tumors was noted in a number of other adequate animal cancer bioassays.

There is some indication that asbestos exposure may have increased the risk of laryngeal cancer in some groups of asbestos workers, but the evidence is not as strong as that for lung cancer and mesothelioma. There is little evidence for the carcinogenicity of asbestos at other sites, although several cases of malignant mesothelioma of the tunica vaginalis testis have been reported in patients with histories of occupational exposure to asbestos.

Several government office and regulatory agencies have considered the evidence regarding the overall carcinogenicity of asbestos. The Department of Health and Human Services (DHHS) has determined that asbestos is known to be a human carcinogen. The EPA has determined that asbestos is a human carcinogen (Group A). In addition, the International Agency for Research on Cancer (IARC) has determined that asbestos is carcinogenic to humans (Group 1). These conclusions are based primarily on the evidence that asbestos causes lung cancer and mesothelioma. A number of researchers and regulatory groups have reviewed the weight-of-evidence on the issue of cancer at other sites after inhalation exposure to asbestos in the workplace, and have reached differing conclusions. For example, some believe that the data constitute substantial evidence that inhalation of asbestos in the workplace does increase risk of cancer at other sites. In contrast, others feel that the evidence is not adequate to reach a firm conclusion, and some believe that the apparent increases in gastrointestinal cancer are probably due to other factors (misdiagnosis, diet, alcohol, disease history, etc.) and cannot be attributed to asbestos. As these conflicting analyses illustrate, when epidemiological studies provide limited evidence for a small increase in cancer risk at a site, it is difficult to distinguish between two alternative interpretations: (1) the risk is real, and inconsistencies in the data are due to limitations in the sensitivity and accuracy of epidemiological studies; or (2) the risk is not real, and the apparent effects are attributable to other causes

or reasons. In view of the limitations and uncertainties in the data available, it does not appear that a definitive distinction can currently be drawn between these alternatives. However, it seems only prudent to consider increased risk of gastrointestinal cancer an effect of concern. This conclusion is similar to that reached by a working group for the U.S. DHHS.

Respiratory Effects. Deposition of asbestos fibers in the lung can lead to substantial nonneoplastic fibrotic injury and may even cause death. This disease, termed asbestosis, results from a prolonged inflammatory response stimulated by the presence of the fibers in the lung. Alveolar macrophages, which normally phagocytize foreign bodies deposited in the lungs, seek to engulf the asbestos fibers and remove them. While short fibers may be cleared in this way, long fibers cannot be removed, and this results in an ongoing focal inflammatory response. With time, some fibers move from the lung to the interstitium where additional inflammatory events take place leading to the development of interstitial pulmonary fibrosis and a progressive loss of lung compliance and respiratory function.

Signs of lung fibrosis and increased mortality associated with asbestosis or nonmalignant respiratory disease have been observed in groups of workers with chronic cumulative exposures as low as 15–70 f-yr/mL for signs of lung fibrosis and 32–1,271 f-yr/mL for asbestosis-associated mortality. The mortality experience associated with asbestosis or nonmalignant respiratory disease in cohorts of exposed workers appears to provide the best available source for describing exposure-response relationships for the development of asbestos-related lung fibrosis. However, a major limitation with the resultant descriptions is that there is very limited information for responses at low levels of exposure experienced by modern workers in regulated nations (<0.1–0.2 f/mL) or at levels experienced in many nonoccupational exposure scenarios ($3x10^{-6}$–$6x10^{-3}$ f/mL). Uncertainty associated with this lack of information may be decreased with results from prospective cohort mortality studies of workers involved in asbestos-related occupations under currently regulated conditions or retrospective studies of workers who entered asbestos-related occupations after 1970 or 1980 when respective occupational limits of 5 and 2 f/mL were recommended in the United States.

Studies of two cohorts of workers exposed to chrysotile asbestos, one from a Carolina textile plant, and the other from Quebec mines and mills, appear to have received the most recent attention by the research and regulatory community because they represent quality studies that provide widely varying estimates of risk for the development of nonmalignant or malignant lung disease associated with the most common type of asbestos. The available data indicate that, at equivalent exposure levels, the risk is greater for textile workers than for miners or millers; these data have been used to develop statistical models that estimate low, but not negligible, risk (2/1,000) for asbestosis-related mortality with chronic exposure to

current occupational exposure limits of 0.1 f/mL. Several authors consider the mortality experience of the Carolina textile cohort to be atypical relative to other asbestos-exposed cohorts and, in the absence of a reliable explanation of this uniqueness, have cautioned against its use in quantitative health assessments for other exposure scenarios to asbestos fibers (see Section 3.2.1.2 for further discussion). Further extrapolation to lower levels of asbestos typically found in ambient air or in the indoor air of homes or public buildings suggests that asbestosis may not be of concern for most people in the general population without occupational exposure to asbestos.

Another tissue that may be affected in humans exposed to asbestos in air is the pleura. The most common effect is the formation of thickened fibrous areas called plaques, but diffuse thickening and fibrosis may also occur, as may areas of pleural effusions. An increased incidence of pleural plaques has been noted at relatively low cumulative exposures (approximately 0.12 f-yr/mL). Localized pleural plaques are not thought to be of significant health concern, although diffuse pleural thickening and circumscribed pleural plaques are associated with impairment of respiratory function. This may also be due to subclinical alveolitis or interstitial fibrosis not detected by routine chest radiograms. These plaques are normally very mild, but may be severe in a few cases probably associated with high exposures.

A few studies have also reported an increased incidence of laryngitis in workers exposed to asbestos. These data suggest that the upper airways may also be affected by asbestos exposure.

Immunological and Lymphoreticular Effects. Studies of workers suffering from asbestos-related diseases such as asbestosis or mesothelioma indicate that the cellular immune system in such patients can be depressed. This is an effect of particular interest and concern since impaired immune surveillance may contribute to the increased incidence of cancer in asbestos-exposed people. Moreover, variation in immune system functional capability might be an important determinant of why some people develop cancer or asbestosis while others, with approximately equal exposures, do not. However, it is very difficult to distinguish whether the alterations in immune function noted in such studies are the cause or the result of asbestos-induced disease. The frequency of impaired cellular immunity in exposed workers without clinically-apparent disease is generally low, although some studies have noted alterations in lymphocyte distribution and impairment of natural killer (NK) cells. This could mean that the immunological changes do not occur until the disease develops (i.e., the changes are the result of the disease). Alternatively, it could mean that workers with immune systems that are not impaired by asbestos do not get serious disease, while workers whose immune systems are injured by asbestos do tend to develop disease (i.e., effects on the immune system are the cause of the disease). Available data do not

allow a firm distinction between these alternatives at present, but the possible immunotoxic effects of asbestos are of clear concern. Results from animal studies provide supporting evidence of direct and indirect effects of asbestos on the immune system, although the specific roles of these effects in the etiology of asbestos-induced pulmonary diseases are not well understood and are under current investigation. For example, experiments with mice indicate that asbestos exposure decreases the number and cytotoxic activity of interstitial pulmonary NK cells and that genetically impaired cell-mediated immunity may be a predisposing factor in asbestos fibrosis.

2.3 MINIMAL RISK LEVELS

Inhalation MRLs

No MRLs were derived for inhalation exposure to asbestos for any duration. Results from epidemiological studies of cohorts of workers chronically exposed to airborne asbestos fiber concentrations ranging from about 5 to 20 f/mL provide convincing evidence of the development of asbestos-induced lung fibrosis, but a chronic MRL was not derived due to the large degree of uncertainty in extrapolating from the available data to levels of exposure that may be several orders of magnitude lower than current U.S. occupational exposure limits (0.1 f/mL). Data regarding the adverse health effects associated with acute- or intermediate-duration exposure to asbestos are lacking or are too limited to support the derivation of an MRL.

Oral MRLs

No MRLs were derived for oral exposure to asbestos for any duration. No studies were located regarding noncancer health effects in humans orally exposed to asbestos fibers, although asbestos cement pipes have been used in some community water systems for many years. Because ingested asbestos fibers are poorly absorbed, the tissue most highly exposed to ingested asbestos is the gastrointestinal tract epithelium. A few studies reported some histological or biochemical changes in gastrointestinal tract cells of rats chronically exposed to oral doses of asbestos, but, in an extensive series of lifetime dietary exposure studies in rats and Syrian hamsters, comprehensive microscopic evaluation of tissues and organs found no excess nonneoplastic lesions in the gastrointestinal epithelium or in other tissues or organs in animals exposed to daily doses as high as 500–830 mg/kg/day. The weight of evidence indicates that asbestos ingestion does not cause any significant noncarcinogenic effects in the gastrointestinal tract or other tissues, and supports the generally held perception that oral exposure to asbestos does not present a high priority public health concern for noncancer effects.