2. RELEVANCE TO PUBLIC HEALTH

2.1 BACKGROUND AND ENVIRONMENTAL EXPOSURES TO SYNTHETIC VITREOUS FIBERS IN THE UNITED STATES

Synthetic vitreous fibers are inorganic substances, primarily composed of aluminum and calcium silicates that are derived from rock, clay, slag, or glass. One of the characteristics that distinguishes these substances from other naturally occurring inorganic fibers is that synthetic vitreous fibers have amorphous molecular structures, while naturally occurring mineral fibers, such as asbestos, possess crystal structures. Synthetic vitreous fibers are broadly classified into three separate categories: fibrous glass; rock wool and slag wool (sometimes collectively referred to as mineral wool); and refractory ceramic fibers. Fibrous glass can either be continuous filament glass fibers (sometimes called textile fibers) or glass wool depending upon how it was produced.

The production and use of synthetic vitreous fibers can cause their release to the environment. Glass wool, rock wool, and slag wool are primarily used in insulating materials for homes, buildings, and appliances. Continuous filament fibers are largely used to reinforce plastics, cement, papers, and roofing materials or woven into industrial fabrics. Refractory ceramic fibers are primarily used in insulating materials that require very high temperature resistence (e.g., furnace insulation). Approximately 80% of the synthetic vitreous fibers produced and used in the United States are glass wool, rock wool, and slag wool. Refractory ceramic fibers only account for about 2% of the total amount of synthetic vitreous fibers produced.

Synthetic vitreous fibers are persistent in the environment because they are not removed by mechanisms that usually degrade organic compounds (e.g., biodegradation, photolysis). Small diameter synthetic vitreous fibers with large surface areas can undergo dissolution, particularly at very high or very low pH levels, but this is more important in biological systems than in the environment (see Section 3.4 for more details regarding dissolution in physiologic fluids). The transport and partitioning of synthetic vitreous fibers in the environment are largely governed by their size. Large fibers are removed from air and water by gravitational settling at a rate primarily dependent on their diameter, but small diameter fibers may remain suspended for longer periods of time before settling down to the ground.

Inhalation exposure to airborne synthetic vitreous fibers is of public health concern because, like other particulate matter, fibers that get suspended in air can be inhaled and deposited in the lung. Depending on the dose, durability, and dimensions of the material, as well as the duration of exposure, the deposited material may lead to lung inflammation and, for the most durable materials, lung tissue cell damage, lung tissue scarring, and cancer of the lung or pleural membrane. Measurements to determine the concentration of synthetic vitreous fibers in air samples are usually reported as the number of fiber(s) per cubic centimeter of air (fiber/cc). Different studies have used different rules for counting fibers in air samples, but in general, a fiber is a particle that has a length $5 µm and a length:diameter ratio (aspect ratio) of $3:1 or $5:1. The World Health Organization (WHO) defines fibers as being >5 µm long, thinner than 3 µm, and having an aspect ratio of $3:1. The National Institute for Occupational Safety and Health (NIOSH) defines fibers as particles with lengths >5 µm and aspect ratios $3:1. A human respirable fiber (a fiber that can be inhaled and reach the lower air-exchange portion of the respiratory tract) is usually defined as a fiber having a diameter of <3 µm. The levels of synthetic vitreous fibers in air are measured by phase contrast microscopy (PCM), transmission electron microscopy (TEM), or scanning electron microscopy (SEM) (see Chapter 7 for more details).

When materials containing synthetic vitreous fibers are physically disturbed, fibers can become suspended in indoor or outdoor air. In general, fibers with small diameters are more easily suspended and remain suspended in air longer than larger-diameter fibers. Among synthetic vitreous fiber types, continuous filament glass fibers usually have the largest average diameters, while refractory ceramic fibers, glass wool, rock wool, and slag wool generally have smaller average diameters (see Chapter 4 for more details). Levels of synthetic vitreous fibers detected in outdoor or indoor air samples are very low, usually on the order of about #0.0001 fiber/cc. In workplaces that manufacture synthetic vitreous fibers, reported air concentrations have mostly been reported to be <0.1–1 fiber/cc. Higher levels have been observed during the installation of insulation in a home or building (respirable airborne levels >1 fiber/cc have been observed); however, these levels quickly fall back to preinstallation levels within 1 or 2 days. The geometric mean concentration of respirable synthetic vitreous fibers ranged from 0.01 to 3.51 fibers/cc at five construction sites where either refractory ceramic fibers, rock wool, or glass wool insulating materials were being installed or removed. The greatest levels were observed during the removal of refractory ceramic fiber insulating material from the inside walls of industrial furnaces, and the lowest levels were observed during the installation of fiberglass panels around ventilation ducts at an industrial construction site.

2.2 SUMMARY OF HEALTH EFFECTS

Reversible acute irritations of the skin, eyes, and upper respiratory tract are well-known health hazards associated with direct dermal and inhalation exposure to refractory ceramic fibers, fibrous glass, rock wool, or slag wool in construction and manufacturing workplaces. Wearing protective clothing and respiratory equipment has been recommended to prevent these health hazards (and possible chronic health hazards) when time-weighted average (TWA) airborne concentrations of fibers exceed recommended occupational exposure limits of 1 fiber/cc for continuous filament glass fibers, glass wool, rock wool, slag wool, and special-purpose glass fibers or 0.2 fibers/cc for refractory ceramic fibers.

Possible health hazards from long-term exposure to airborne refractory ceramic fibers, fibrous glass, rock wool, or slag wool include effects associated with occupational exposure to asbestos (pulmonary or pleural fibrosis [i.e., tissue scarring], lung cancer, and pleural or peritoneal mesothelioma), but available evidence from epidemiologic and animal studies indicates that these materials, as a class, are much less potent than asbestos. Epidemiological studies of workers involved in the manufacture of fibrous glass, rock wool, or slag wool have found no consistent evidence for exposure-related increased risks of dying from nonmalignant respiratory disease, lung cancer, or mesothelioma. Results from animal studies indicate that high-level inhalation exposure to any synthetic vitreous fiber may cause reversible pulmonary inflammation, but only the most biopersistent of synthetic vitreous fibers have been demonstrated to produce irreversible pleural or pulmonary fibrosis, lung cancer, or mesothelioma. Health effects at other target organs are not expected from exposure to airborne synthetic vitreous fibers.

Mechanistic and pharmacokinetic studies with asbestos and synthetic vitreous fibers indicate that greater potential for toxicity of inhaled inorganic fibers is associated with higher exposure concentrations, longer exposure durations, longer fiber lengths, greater fiber durability, and thinner fiber diameters. As discussed in Sections 3.4 and 3.5, fiber dimensions influence several of these key determinants of toxicity including:

(1) the amount of material deposited in the alveolar region of the lung (fibers with diameters >3 µm do not reach this region; they are deposited in the upper respiratory tract and lung conductive airways, cleared by mucociliary action to the pharynx, swallowed, and eliminated via the feces);

(2) the rate at which macrophages engulf and clear fibers deposited in the lower lung (human macrophages cannot fully engulf fibers with lengths longer than about 15–20 µm); and

(3) the extent of movement of deposited fibers from the alveoli to the lung interstitium and the pleural cavity (fibers with diameters >0.3–0.4 μm may move less freely into the interstitium and pleural cavity).

Fibers that can dissolve in physiologic fluids (i.e., that are less durable) develop weak points that can facilitate (1) transverse breakage by physical forces into shorter fibers and (2) faster clearance by macrophages, compared with fibers that do not dissolve, like amphibole asbestos fibers.

Synthetic vitreous fibers differ from asbestos in two ways that may provide at least partial explanations for their lower toxicity. Because most synthetic vitreous fibers are not crystalline like asbestos, they do not split longitudinally to form thinner fibers. They also generally have markedly less biopersistence in biological tissues than asbestos fibers because they can undergo dissolution and transverse breakage (see Sections 3.4 and 3.5).

Irritation Effects. Occupational exposure to fibrous glass materials, including glass wool insulation and fiberglass fabrics, has been associated with acute skin irritation ("fiberglass itch"), eye irritation, and symptoms of upper respiratory tract irritation such as sore throat, nasal congestion, laryngeal pain, and cough. The skin irritation has been associated with glass wool fibers having diameters >5 μm and becomes less pronounced with continued exposure. Symptoms of irritation of the upper respiratory tract have been mostly associated with unusually dusty workplace conditions (concentrations >1 fiber/cc) involving removal of fibrous glass materials in closed spaces without respiratory protection. The symptoms have been reported to disappear shortly following cessation of exposure. Similar symptoms of dermal and upper respiratory irritation may also occur in workers involved in the manufacture, application, or removal of insulation materials containing refractory ceramic fibers, rock wool, or slag wool.

Cancer and Nonmalignant Respiratory Disease. Studies of populations working with fibrous glass materials have focused on the prevalence of respiratory symptoms through the administration of questionnaires, pulmonary function testing, and chest x-ray examinations. In general, these studies reported no consistent evidence for increased prevalence of adverse respiratory symptoms, abnormal pulmonary functions, or chest x-ray abnormalities; however, one study reported altered pulmonary function (decreased forced expiratory volume in 1 second) in a group of Danish insulation workers compared with a group of bus drivers. These studies, while informative, do not account for workers who had ceased exposure before the study and provide no information regarding possible exposure-response relationships.

Longitudinal health evaluations of workers involved in the manufacture of refractory ceramic fibers, fibrous glass, rock wool, or slag wool have not found consistent evidence of changes in chest x-rays or pulmonary functions, with the exception that pleural plaques were found in about 3% of examined U.S. refractory ceramic fiber manufacturing workers.

Epidemiologic studies (cohort mortality and case-control studies) of causes of mortality among groups of workers involved in the manufacture of fibrous glass, rock wool, or slag wool provide no consistent evidence for increased risks of mortality from nonmalignant respiratory disease, lung cancer, or pleural mesothelioma. A number of reviews of these cohort mortality and case-control studies concur that the studies provide inadequate evidence for the carcinogenicity of synthetic vitreous fibers in humans. Similar cohort mortality or case-control studies of workers involved in the manufacture of refractory ceramic fibers have not been conducted.

For all synthetic vitreous fibers tested, pulmonary inflammation has been observed in animals (predominately rodents) following intermediate- or chronic-duration inhalation exposure at concentrations more than an order of magnitude higher than 1 fiber/cc. This concentration is the current occupational exposure limit for synthetic vitreous fibers recommended by the American Conference of Governmental Industrial Hygienists. The most extensively studied refractory ceramic fiber, RCF1, caused minimal-to-mild pulmonary inflammation in rats and hamsters at concentrations as low as 36 fibers/cc at 3 months. The severity of inflammation increased with duration and exposure concentration, but the severity of inflammatory lesions did not exceed a moderate rating of “3" in most rats (on a 0–4 grade scale where 0 was “normal” and 4 was “marked”) even with exposure for 24 months to a concentration of 234 fibers/cc. The inflammation showed signs of regression after cessation of exposure. Other refractory ceramic fibers, RCF2, RCF3, and RCF4, caused minimal-to-mild pulmonary inflammation in rats at single exposure levels in the concentration range of 206–268 fiber/cc. The insulation glass wool MMVF10 caused pulmonary inflammation at concentrations as low as 36 WHO fibers/cc in hamsters and rats. Other multiple-exposure tests in male rats have demonstrated the induction of minimal pulmonary inflammation from concentrations as low as 46 fibers/cc of the glass wool, MMVF11, 44 fibers/cc of the rock wool, MMVF21, and 33 fibers/cc of the slag wool, MMVF22. Several of these studies also showed that signs of inflammation subsided to various degrees after cessation of exposure.

Pulmonary inflammation has also been observed in single-concentration experiments in male rats following intermediate- or chronic-duration inhalation exposure to the durable glass fiber, MMVF33, at

318 WHO fibers/cc, the high-temperature stone wool, MMVF34, at 400 fibers/cc, the high-silica synthetic vitreous fiber, X607, at 180 fibers/cc, the special-purpose microfiber, 104E-glass, at 1,022 fibers/cc, and GB100R glass wool at 2.2 mg/m^3 (concentration expressed as fiber number per cc was not reported). An intermediate-duration study in male baboons reported that, 1,122 fibers/cc of C102/C104 blend fibrous glass induced pulmonary inflammation. The only study to report a no-observed-adverse-effect-level (NOAEL) for pulmonary inflammation exposed female Wistar rats to 576 fibers/cc of Code 104 glass wool for 12 months.

Pulmonary or pleural fibrosis has been observed in animals following intermediate- or chronic-duration inhalation exposure to several refractory ceramic fibers, RCF1, RCF2, RCF3, and RCF4, in the concentration range of 208–268 fibers/cc, the durable (i.e., biopersistent) glass fiber, MMVF33, at 310 WHO fibers/cc, the insulation rock wool, MMVF21, at 185 fibers/cc, the special microfiber, 104E-glass, at 1,022 fibers/cc, and C102/104 blend fibrous glass at 1,122 fibers/cc. Dose-response relationships for pulmonary or pleural fibrosis are best described, among these “fibrotic” synthetic vitreous fibers, for the refractory ceramic fiber, RCF1. In rats exposed to RCF1 for up to 2 years, signs of irreversible pulmonary or pleural fibrosis were induced at concentrations >91 fibers/cc, but not at 36 fibers/cc. In general, synthetic vitreous fibers that cause fibrosis are more biopersistent than those that do not.

Synthetic vitreous fibers that have not induced pulmonary or pleural fibrosis in animals following intermediate- or chronic-duration inhalation exposure include the insulation glass wools, MMVF10 and MMVF11, at concentrations in the 273–339 fibers/cc range, the slag wool, MMVF22, at 245 fibers/cc, the high-temperature stone wool, MMVF34, at 400 fibers/cc, and the high-silica synthetic vitreous fiber, X607, at 180 fibers/cc.

Chronic inhalation exposure of animals to several biopersistent synthetic vitreous fibers has been shown to induce lung tumors or mesothelioma, whereas several less biopersistent synthetic fibers have not induced tumorigenic responses in animals exposed by inhalation for chronic durations. In these experiments, statistically significant increases in lung tumor incidence (adenomas or carcinomas) have been accepted as evidence of a tumorigenic response, whereas any detection of a mesotheolioma has been generally accepted as evidence for this relatively rare type of tumor.

Tumorigenic responses in the lung or pleura have been observed in hamsters and rats exposed to the refractory ceramic fiber, RCF1, at concentrations as low as 91 fibers/cc, in rats exposed to RCF2, RCF3, or RCF4 at concentrations between 206 and 268 fibers/cc, in hamsters exposed to the durable glass fiber, MMVF33, at 256 fibers/cc, and in rats exposed to the special applications microfiber, 104E-glass, at 1,022 fibers/cc. The carcinogenic response to 104E-glass in rats was observed after only 1 year of exposure, in contrast to another special purpose glass microfiber, 100/475, which did not induce cancer in rats exposed to 1,022 fibers/cc for 1 year.

No other synthetic vitreous fiber types have exhibited evidence of carcinogenicity in chronic inhalation animal testing. Neither increased lung tumor incidence or the presence of mesotheliomas were found in rats exposed for 2 years to: the insulation glass wools, MMVF10 or MMVF11 at 287 or 273 fibers/cc; the insulation rock wool, MMVF21, at 264 fibers/cc of MMVF21; the slag wool, MMVF22, at 245 fibers/cc; the high-temperature stone wool, MMVF34, at 400 fibers/cc; or the high-silica synthetic vitreous fiber, X607, at 180 WHO fibers/cc. Additionally, evidence for carcinogenic responses was not found in male hamsters exposed to MMVF10 at 339 WHO fibers. Although no tumors were found in male baboons exposed to 1,122 fibers/cc of C102/C104 blend fibrous glass for 30 months, the study was limited by small study size (biopsies of only two animals).

Increased incidences of fibrosis or tumors (e.g., lung tumors, mesotheliomas, sarcomas, or abdominal cavity tumors) have been observed in studies of rodents exposed to glass wool, rock wool, slag wool, or refractory ceramic fibers by intratracheal instillation, by intrapleural implantation or injection, and by intraperitoneal injection. These lesions were not observed in a few studies involving intraperitoneal injection of continuous filament glass fibers. Most of these studies involve a single administration followed by observation periods up to 2 years. The relevance of these studies to human inhalation exposure is limited because of the high doses used, the bypassing of the natural defense systems of the nasal and upper respiratory system, and the overloading or lack (for intraperitoneal studies) of clearance mechanisms mediated by pulmonary macrophages.

The U.S. Department of Health and Human Services, National Toxicology Program classified glass wool (respirable size) as *reasonably anticipated to be a human carcinogen*, based on sufficient evidence of carcinogenicity in experimental animals. This assessment was originally listed in the *7th Report on Carcinogens*, but has not been updated since then in the *8th or 9th Reports on Carcinogens*. Continuous filament glass, rock wool, slag wool, or refractory ceramic fibers were not listed or assessed for carcinogenicity in the *9th Report on Carcinogens*.

In 2001, the International Agency for Research on Cancer (IARC) convened a scientific working group of 19 experts from 11 countries to review a new monograph on "man-made vitreous fibers" that will replace the previous IARC (1988) monograph on these materials. However, as of June 2002, the monograph had not been published, and the *List of IARC Evaluations* on IARC's Web site (http://193.51.164.11/monoeval/grlist.html) had not been updated to reflect the new classifications noted below. As reported in an IARC (2001) press release, the new monograph and the working group concluded that epidemiologic studies published since the previous IARC (1988) assessment provide no evidence of increased risks of lung cancer or of mesothelioma from occupational exposure during the manufacture of man-made vitreous fibers and inadequate evidence overall of any excess cancer risk. Insulation glass wool, rock (stone) wool, slag wool, and continuous filament glass were classified in Group 3, *not classifiable as to carcinogenicity to humans* because of the inadequate evidence of carcinogenicity in humans and the relatively low biopersistence of these materials. In contrast, refractory ceramic fibers and certain special-purpose glass wools not used as insulating materials were classified in Group 2B*, possibly carcinogenic to humans,* because of their relatively high biopersistence.

The U.S. EPA Integrated Risk Information System (IRIS) has not classified the potential carcinogenicity of glass wool, continuous filament glass, rock wool, or slag wool, but assigned refractory ceramic fibers to Group B2, *probable human carcinogen*, based on no data on carcinogenicity in humans and sufficient evidence of carcinogenicity in animal studies. Currently, EPA is developing a cancer assessment for refractory ceramic fibers based on recent multiple-exposure chronic inhalation animal bioassays. The assessment is considering the development of quantitative inhalation unit risk estimates for refractory ceramic fibers based on the animal tumorigenic responses, but, as of June 2002, the assessment is not completed.

2.3 MINIMAL RISK LEVELS

Inhalation MRLs

- A minimal risk level (MRL) of 0.03 fibers/cc has been derived for chronic-duration inhalation exposure to refractory ceramic fibers.

The 2-year, multiple-exposure level inhalation bioassay of the refractory ceramic fiber, RCF1, in male Fischer 344 rats provides the best available data describing dose-response relationships for nonneoplastic lesions in the lung and pleura from chronic inhalation exposure to refractory ceramic fibers. The study identifies pulmonary inflammation as the critical nonneoplastic end point of concern and identifies other more serious effects at higher exposure levels (pulmonary and pleural fibrosis and cancer of the lung and pleura). Other studies of rats exposed to RCF1 by inhalation provide strong support for pulmonary inflammation as the critical end point (Bellman et al. 2001; Everitt et al. 1997; Gelzleichter et al. 1999; McConnell et al. 1995), as well as other animal inhalation studies of other refractory ceramic fibers (Mast et al. 1995a) and other synthetic vitreous fibers such as insulation glass wools, MMVF10 and MMVF11 (Hesterberg et al. 1993c; McConnell et al. 1999), slag wool MMVF22 (McConnell et al. 1994), and rock wool MMVF21 (McConnell et al. 1994).

There are distinct differences between laboratory animal species and humans in respiratory tract size and geometry, ventilation rats and pattern, and macrophage sizes that influence the retention (the net result of deposition and clearance) of fibers in the lung. Yu and colleagues (Yu et al. 1995a, 1995b, 1996, 1997, 1998a, 1998b) have developed lung retention models for RCF1 in rats and humans that incorporate many of these interspecies differences. These models significantly decrease uncertainty in extrapolating doses from rats to humans.

In deriving the MRL, the models were used to convert the rat exposure levels in the Mast et al. (1995a, 1995b) bioassay to human equivalent concentrations (see Appendix A for more details). The human equivalent concentrations and data for three indicators of pulmonary inflammation (lung weight, macrophage aggregation score, and bronchiolization score) were modeled with four continuous-variable models available in the EPA Benchmark Dose Software. The derivation assumes that rats and humans are equally sensitive to the inflammatory effects of refractory ceramic fibers. Macrophage aggregation score was selected as the most sensitive of these indicators to serve as the basis of the MRL. The point of departure for the MRL was the approximate median value (1 fiber/cc) of 95% lower limits on predicted concentrations (from several models) associated with an average score for minimal pulmonary macrophage aggregation. This value of 1 fiber/cc was divided by an uncertainty factor of 30 (3 for extrapolation from rats to humans with dosimetric adjustment and 10 for human variability) to arrive at the MRL of 0.03 fiber/cc.

Available comparative data with other refractory ceramic fibers (e.g., data for RCF2, RCF3, and RCF4 reported by Mast et al. 1995a) suggest that RCF1 is as potent or more potent than other refractory ceramic fibers. Thus, the chronic MRL based on RCF1 data is expected to be protective of the public health for exposure to other refractory ceramic fibers. In addition to its relatively high durability, a contributing factor to the high potency of RCF1 relative to other refractory ceramic fibers is the high content of nonfibrous particles in RCF1. Bellmann et al. (2001) have reported that the mass concentration of total fibers (particles with aspect ratio >3:1) and nonfibrous particles (with aspect ratios <3:1) in RCF1 are 0.76 and 0.26 ng/ng RCF1, respectively. Some evidence that the presence of the nonfibrous particles can enhance the effects on the lung was provided by comparing responses in rats exposed by inhalation for 3 weeks to concentrations of about 125 fibers (with lengths >20 μm)/cc of either RCF1 or a sample of refractory ceramic fiber, called RCF1a, in which only 2% of the mass was accounted for by nonfibrous particles (Bellmann et al. 2001). Expressed as WHO fibers/cc, the mean concentrations were 481 fibers/cc for RCF1a and 679 fibers/cc for RCF1. Pulmonary clearance ability was markedly depressed by RCF1, but not by RCF1a, and indices of pulmonary inflammation were more persistently increased by RCF1 than by RCF1a (Bellmann et al. 2001).

The chronic MRL is also expected to be appropriately applied to intermediate-duration exposure scenarios, based on evidence from interim sacrifice data from the Mast et al. (1995a, 1995b) bioassay that exposure-response relationships for pulmonary inflammation and chronic exposure are similar to those for intermediate-duration exposure. Scores for pulmonary inflammation progressed to only a limited degree with progression from intermediate to chronic duration. For example, mean scores for macrophage aggregation in rats exposed to 3, 9, 16, and 30 mg/m^3 at 3 months were 1.7, 2, 2, and 2, respectively. At 12 and 24 months, the respective scores were: 2, 2.3, 3, and 3; and 2, 2.5, 3, and 3.2.

Dose-response relationships for pulmonary inflammation from acute inhalation exposure to synthetic vitreous fibers are inadequately characterized for deriving an acute inhalation MRL for any type of synthetic vitreous fiber.

Any use of the MRL for refractory ceramic fibers in assessing likely health hazards from the insulation wools should acknowledge the evidence that many of the insulation wools are markedly less durable and less potent than refractory ceramic fibers (Bernstein et al. 2001a, 2001b; Eastes and Hadley 1996; Eastes et al. 2000; Hesterberg et al. 1998a). There are data from multiple-exposure-level 2-year rat inhalation bioassays on the glass wools, MMVF10 and MMVF11 (Hesterberg et al. 1993c; McConnell et al. 1999), the slag wool, MMVF22 (McConnell et al. 1994), and the rock wool, MMVF21 (McConnell et al. 1994) that adequately describe dose-response relationships for nonneoplastic pulmonary effects (i.e., pulmonary inflammation) from intermediate- and chronic-duration exposure to these materials. However, lung retention models for these synthetic vitreous fibers are not yet fully developed to carry out physiologically based dosimetric calculations of human equivalent concentrations.

There are no adequate data (from multiple-exposure level studies) for deriving inhalation MRLs for the other types of synthetic vitreous fibers (special applications glass fibers or continuous filament glass fibers that are woven).

Oral MRLs

No MRLs were derived for oral exposure to any synthetic vitreous fibers for any duration of exposure. No studies were located regarding noncancer health effects in humans or animals orally exposed to synthetic vitreous fibers. Oral exposure to synthetic vitreous fibers does not present a high priority public health concern, given the low probability of exposure by this route. Supporting the lack of concern, results from an extensive series of lifetime studies of asbestos fibers in the diet of rats and hamsters found no consistent evidence for increased nonneoplastic lesions in exposed compared with control animals (see Agency for Toxic Substance and Disease Registry 2001).