establishing a dose-response relationship between asbestos exposure and an excess risk of either lung cancer or mesothelioma is exceptionally strong. The following studies have shown a positive dose-response relationship for an increased risk of lung cancer mortality and/or mesothelioma mortality: Finkelstein (Ex. 84–240), Dement et al. (Ex. 84–036, 84–037), Henderson and Enterline (Ex. 84–048), Seidman (Ex. 261–A), Berry and Newhouse (Ex. 84–021), Weill et al. (Ex. 84–206), Selikoff et al. (Ex. 84–87), and Peto (Ex. 84–169). OSHA has used these studies in its Quantitative Risk Assessment (see Section V) to show that cumulative exposure levels below that permitted by the existing PEL of 2 f/cc presents an excess risk of cancer mortality.

These studies also show that cumulative exposure levels of asbestos below that permitted by lifetime exposure to the 2 f/cc PEL results in excess mortality from lung cancer and mesothelioma. Furthermore, the Seidman update (Ex. 261–A) and the Nicholson and Selikoff study (Ex. 162–C) clearly indicate that workers exposed for a relatively short period of time experienced significant excess mortality from lung cancer and from all asbestos diseases. OSHA believes that the results of Zoloth and Michael's study (Ex. 163–E) of asbestos-exposed sheetmetal workers further suggests that excess mortality can occur from intermittent exposure conditions. In light of the findings of these three new studies (Exs. 162–C, 163–E, 261–A) and the previously considered evidence, OSHA concludes that well-conducted studies demonstrate a substantially increased rate of lung cancer and mesothelioma mortality among workers having low cumulative exposures to asbestos.

C. Carcinogenicity of Asbestos for Sites Other than the Lung and Mesothelium

1. Epidemiological Studies

In the November proposal, OSHA reviewed several epidemiological studies describing the mortality experience of asbestos-exposed occupational cohorts in regard to cancer occurring at sites other than the lung and mesothelium. Seven studies were reviewed that found statistically significant increases in deaths from gastrointestinal cancer among U.S. and Canadian insulation workers (Exs. 84–090, 84–224), Belfast insulation workers (Exs. 84–041, 84–090), asbestos factory workers (Exs. 84–048, 84–330), shipyard workers (Ex. 84–246), and tremolite and anthophyllite-exposed talc miners (Exs. 84–140, 84–141). Of these studies, the most striking is the investigation of 17,800 U.S. and Canadian insulation workers conducted by Selikoff, Hammond, and Seidman (Ex. 84–090). In this study, significant excess mortality was observed from lung cancer (SMR=406), mesothelioma (180 deaths), esophageal cancer (SMR=253), stomach cancer (SMR=126), colo-rectal cancer (SMR=152), laryngeal cancer (SMR=191), pharyngeal and buccal cavity cancer (SMR=159), kidney cancer (SMR=223), prostate cancer (SMR=137), and non-infectious respiratory diseases including asbestosis (SMR=319).

Selikoff, Hammond, and Seidman concluded:

> Asbestos insulation workers in the United States and Canada suffer an extraordinary increased risk of death of cancer and asbestosis associated with their employment. This includes increases in deaths from lung cancer, pleural mesothelioma, peritoneal mesothelioma, cancer of the esophagus, colon and rectum, cancer of the larynx, oro-pharynx, kidney, and perhaps stomach. Some increases were seen in cancer of several other sites, as well, but data are inadequate at this time to permit characterization of their significance although attention is called to such wider increase (Ex. 84–090, p. 114).

In addition to the above-mentioned studies, OSHA reviewed five studies that showed non-statistically significant increases in gastrointestinal tract cancer. The occupational cohorts examined in these studies included chrysotile textile plant workers (Ex. 84–090, p. 114), chrysotile miners and millers (Ex. 84–065), amosite insulation production workers (Ex. 84–087), and asbestos factory workers (Exs. 84–251, 84–082). The November 1983 notice also pointed out that several epidemiological studies failed to find any excess of gastrointestinal cancer among friction material production workers; chrysotile, anthrophyllite, and talc miners, chrysotile factory workers, asbestos gas mask workers, asbestos textile workers, and shipyard workers.

In summary, 12 different epidemiological studies of a variety of occupational cohorts exposed to asbestos have found excess mortality from gastrointestinal cancers; of these, 7 studies found statistically significant excesses. OSHA believes that these findings constitute substantial evidence of an association between asbestos exposure and a risk of incurring gastrointestinal cancer.

2. Experimental Studies

In the November proposal, OSHA discussed a number of toxicological studies conducted on animals to determine the carcinogenicity of ingested asbestos. A study conducted by Ward et al. (Ex. 84–200) found that 32 percent of amosite-treated Fischer 344 rats developed colon carcinoma; a fairly high incidence of colon tumors compared with the incidence among historical controls from the same laboratory.

Two studies show evidence of gastrointestinal tumors developing in chrysotile and amosite-treated animals but not in the control animals (Bolton et al. Ex. 84–214; Smith et al., Ex. 84–193). However, these results were considered questionable by the authors because, in the case of the Smith et al. study (Ex. 84–193), other investigators observed the same types of tumors in the animal strain studied and, in the case of the Bolton et al. study (Ex. 84–214), asbestos fibers were not found in the mesenteric lymphatic tissue of the amosite-treated animals that developed benign tumors.

However, several studies reported no significant increases in tumor incidence after the administration of chrysotile, amosite, tremolite, and crocidolite asbestos orally to laboratory animals; these studies included those conducted by the National Toxicology Program (NTP) (Exs. 84–225, 84–226, 84–227, and 84–228) and by Donham et al. (Ex. 84–222). In the NTP studies doses well below the maximum tolerated dose (1 percent of diet) were administered, and in some of the NTP studies, relatively short fibers were administered. Although the study by Donham et al. failed to show a significant increase in tumorigenesis, the authors believed that their results showed a trend towards increased colon lesions.

Since the November proposal OSHA has reviewed an additional lifetime feeding study of amosite-treated rats. McConnell et al. (Ex. 306) administered amosite asbestos (1 percent of diet) to a group of 250 8-week-old male and female Fischer 344 rats. When animals were examined for tumors, the incidence of gastro-intestinal tumors among treated male and female rats (7/249 and 4/250, respectively) was found to be comparable to that of untreated male and female controls (4/117 and 2/117, respectively). Treated male rats were found to have a significantly higher incidence of C-cell carcinoma (50/246), compared to male controls (11/117), but due to the lack of other significant findings, the authors did not attribute the increase in the incidence of C-cell carcinoma among treated male rats to amosite exposure.

Although OSHA finds that results from ingestion studies are equivocal and inconsistent with respect to the carcinogenic potential of exposure to

GLEASON-000868