fluctuations caused by the small size of the cohort or the possible confounding effects of smoking may have been responsible for this unexpected result. More likely, lung cancer risk may have been underestimated for the highest exposure category by Finkelstein's exclusion of any lung cancer deaths that might have occurred during the 20 years from onset of exposure to the beginning of the followup period. In addition to showing dose-response relationships between asbestos exposure and the excess risk from lung cancer and mesothelioma, OSHA notes that Finkelstein's study presents evidence that an excess risk for these diseases exists at cumulative exposures that would be permitted by lifetime exposure to the 2-fcc standard.

Rubino et al. (Ex. 84–086) studied the mortality of 952 male Italian chrysotile miners and millers. The mortality experience of the overall cohort was compared with that of nonexposed Italian males. Compared with nonexposed Italians, the overall cohort had statistically significant excesses of mortality from laryngeal cancer, nonmalignant respiratory diseases, and non-asbestos-related causes, but not from lung cancer. However, there were some trends showing increasing lung cancer risk with increasing length of followup and increasing cumulative exposure. Using the methodology presented in Ex. 84–336, OSHA determined that this study had only a 33.5 percent power to detect a 50 percent increase in lung cancer risk among workers with 20 or more years of followup. Generally, it is considered desirable for studies to have at least an 80 percent power to detect a 50 percent increase in disease.

Weill et al. (Ex. 84–206) studied mortality among 5,645 men having at least 20 years of latency since first exposure in either of two asbestos cement plants. Each worker's cumulative dust exposure during the 20 years after the onset of exposure was estimated in terms of mpcf-years. Based on the conversion factor of 1:1.4 suggested by Hammad et al. Ex. 84–277), the five cumulative exposure categories would be equivalent to 14 or fewer f/cc-years, 15–70 f/cc-years, 71–140 f/cc-years, 141–280 f/cc-years, and 281 or more f/cc-years. Neither respiratory cancer mortality nor any other cause of death was increased among workers in the three lowest exposure categories. Weill et al. noted that the relatively high proportion (25 percent) of the cohort that was lost to followup and assumed to be alive may have led to an underestimation of respiratory cancer risk. The upper limits of the 95 percent confidence intervals of the SMRs for respiratory cancer for the three lowest exposure categories ranged from approximately 115 to 150, indicating, in OSHA's opinion, that the presence of an excess risk of mortality from lung cancer could not be ruled out for the cohorts in these exposure categories.

Berry and Newhouse (Ex. 84–021) studied the mortality of a large cohort of friction material production workers whose asbestos exposures were relatively low (generally less than 1 f/cc to 5 f/cc) and of short duration. Cumulative exposures for the cohort averaged less than 50 f/cc-years. Only non-significant increases in mortality from lung cancer were observed; however, mortality from mesothelioma was significantly elevated compared with that of controls. Most of the mesothelioma victims had been exposed to asbestos levels exceeding 5 f/cc; their cumulative exposure estimates were not reported. A sizeable portion of the cohort was studied for a relatively short followup period between onset of exposure and the end of the study. For example, the followup period for 33 percent of the men was less than 20 years. Because of the short followup period used, OSHA does not believe that the non-significant increases in lung cancer mortality found by these investigators contradict the findings from other studies, which show that low-level exposure to asbestos has resulted in excessive mortality from lung cancer.

Of the few epidemiologic studies submitted to the docket after the publication of the November proposal, four provide additional information on the risk of lung cancer mortality and/or mesothelioma mortality among workers exposed to asbestos. The first (Cantor, Ex. 168–A; Cantor et al., Ex. 168–B) is only an interim report on a proportionate mortality study and has no estimates of cumulative exposure. Two other studies similarly give no estimates of cumulative exposure; one (Nicholson and Selikoff, Ex. 162–C) investigates the risks of recent exposures of limited duration, while another (Zoloth and Michaels, Ex. 163–E) investigates the effects of intermittent asbestos exposure. The fourth study (Seidman, Ex. 261–A) is an update of a previous study (Seidman et al., Ex. 84–087) and was discussed earlier in this section.

Kenneth P. Cantor, of the National Cancer Institute, submitted an interim report (Ex. 168–A; Cantor et al., Ex. 168–B) on his proportionate mortality study of 7,121 deaths identified among members and retirees of the California local of the United Association of Plumbers and Pipefitters. The interim report was based on 6,398 (89.8 percent) of the 7,121 deaths. No specific information was available on cigarette smoking habits or on asbestos exposure levels. Expected numbers of deaths were calculated from cause-specific proportionate mortality rates by 5-year age and 5-year calendar period groups among U.S. white males. For mesothelioma, the expected number of deaths was estimated on the basis of death certificate information for approximately 10 percent of the U.S. population. Further analysis conducted after the interim report confirms the interim report findings (Ex. 168–A).

The most striking finding from this report is that 15 mesothelioma deaths occurred in this group, while only 2 were expected. A significant (p less than 0.05) excess number of lung cancer deaths was also observed (587 observed, 408 expected). Other smoking-related cancer sites had PMRs at or near expected levels. The investigators concluded:

> "It is likely that exposure to asbestos is responsible for at least part, if not all, of the excess number of lung cancers in this group:
>
> 1. The excessive number of deaths due to lung cancer is consistent with the elevated number of mesothelioma deaths that points to widespread asbestos exposure.
>
> 2. If cigarette smoking *had* [emphasis added] played an important role in causing excess lung cancer deaths, we would expect the PMR for bladder cancer, another smoking-related . . . [malignancy] that has not been linked to asbestos exposure, to also be elevated. There were 40 deaths due to bladder cancer whereas 40.4 were expected (PMR=.99), suggesting no increase in risk for cancers of this site." (Ex. 168–A, pp. 3–4.)

This study, although it is an interim report, is significant for two reasons. First, the excess number of deaths from mesothelioma add to the already considerable weight of evidence for a causal relationship between asbestos exposure and an increased mortality risk from this rare cancer. Second, despite the lack of data on smoking habits for the cohort, the study suggests that asbestos exposure, and not smoking, was the principal cause of the observed excess in lung cancer mortality.

Nicholson and Selikoff (Ex. 162–C) investigated mortality among 1,918 male shipyard workers who were employed on January 1, 1967 and who were first employed before January 11, 1957. More than 80 percent of the cohort was employed for less than 20 years. Although no estimates of exposure levels were given, the authors state that: "in terms of time from onset of exposure

GLEASON-000866