As pointed out by Dr. Weill in his written testimony, "Exposure-response relationships have been reported using as the biologic response indicator either a constellation of clinical findings to define asbestosis, or certification by a worker's compensation panel or board" [Ex. 99, p. 24], but such approaches have "varying degrees of limitation" [Ex. 99, p. 12]. Because of the many possible combinations, and therefore "definitions" of asbestosis given by different groups, the quantification of a single risk associated with asbestosis is difficult. As Dr. Weill noted during cross examination:

> • • • The problem is with asbestosis, the quantification is not exactly the same as it is with malignant disease; because one is dealing with a different set of rules in the ascertainment of this health effect. And no two studies have exactly the same scheme for making a decision that this individual has asbestosis and this individual doesn't [Tr. 6/19, pp. 205–206].

In his preheaving testimony, Dr. Weill explained further:

> Mortality data are not useful in quantifying the risk of asbestos-induced lung fibrosis (asbestosis). Affected workers may die with asbestosis but not of it, in which case it is not likely to appear on the death certificate as the primary cause of death. In contrast, sensitivity of detecting early evidence of asbestosis in a living exposed population has increased substantially in recent years. . . . Since much of the asbestosis being seen now is the result of lower dust levels in the past two decades, the films are likely to be classified in the lower categories of profusion of small opacities (fewer shadows meaning less severe disease). As is frequently the case with biological measurements, it is at these lower limits of disease detection that inter- and intra-observer variability is greatest. Again, it is gratifying to know that in spite of these recognized problems, excellent exposure-response relationships have resulted from the radiographic classification described [Ex. 99, 23].

Quantitative studies exist, primarily for the disabling forms of the disease; specifically, two separate studies provide information to develop a dose-response relationship between asbestos exposure and incidence of asbestosis [Ex. 84–254 and 84–44.] Details of the data were reported at 48 FR 51130. It is clear that material impairment from asbestosis occurs prior to the onset of its disabling stage.

As discussed in the November proposal, Berry et al. [1979; Ex. 84–20] studied a group of 379 men who worked at an asbestos textile factory for at least 10 years. Dust measurements were available and were correlated to each job performed for each year under study. Health effects were correlated to cumulative exposure. Using prevalence data, Berry et al. found a dose-response relationship with cumulative exposure (f-y/cc) for three endpoints, crepitations, possible asbestosis, and certified asbestosis. In addition, these data also support the hypothesis that there is a low, or possibly no, threshold for asbestosis, since there is increased risk at cumulative exposures as low as 37 fiber-years/cc.

Berry and Lewinsohn [1979, Ex. 84–254] have reported the incidence of asbestosis in this same asbestos textile factory. The population was divided into two cohorts: those first employed before 1951 and those employed after 1950. A dose-response relationship is apparent for the incidence data, though it is not quite as consistent as for the prevalence data.

In a second study, Finkelstein [1982, Ex. 84–44] looked at the development of compensable (certified) asbestosis among 201 workers at an asbestos-cement factory in Ontario. A dose-response relationship was developed using estimated cumulative exposures based on plant dust measurements and using medical information from the Ontario Workmen's Compensation Board.

As noted by Dr. Weill, "A final complicating aspect in the development of exposure-response information on asbestosis is that it is a slowly progressive disorder which may (and frequently does) continue to worsen after exposure ceases" [Ex. 99, p. 12].

OSHA's original estimates of risk were derived from a simple linear regression of the incidence of asbestosis on the midpoints of the cumulative exposure data of Berry and Lewinsohn and of Finkelstein. A linear relationship was assumed, at least for the point estimation of 0.5 fibers/cc for 45 years (or 22.5 fiber-years/cc). As Dr. Weill stated:

> While the shape of the dose-response curve for asbestosis cannot be determined with certainty, it is clear that this fibrotic effect is dose-related, perhaps linearly, and whether a threshold exists may very well depend on the response indicator chosen [Ex. 99, p. 11].

The assumption of risk linearity is consistent with the fact that early stages of the disease are observed at low exposures. This point was reiterated by Howard Ayer on behalf of the Organization Resources Counselors, Inc. when he noted that:

> It does appear clear that there is a simple linear relationship between the frequency and degree of asbestosis and the cumulative exposure to asbestos dust. Time is merely a factor in that it takes a certain amount of time—at least a matter of years—to develop the effect on the lung [Ex. 91–10–2, pp. 4–5].

A similar conclusion is drawn in the report of the British Advisory Committee on Asbestos, when the committee noted that: "The present authors come down in favor of a dose-response relationship [asbestosis] without a threshold for chrysotile within the range experienced in industry" [Ex. 84–216, volume 2, p. 38]. Based on this recommendation, OSHA did employ a linear model in the prediction of risk from asbestosis, but made no attempt in the proposal to extrapolate the data below the 0.5 f/cc level or above the 10 f/cc level using this model.

Based on the three cohorts discussed above, OSHA calculated estimates of the lifetime incidence of asbestosis for the Finkelstein, Berry and Lewinsohn pre-1951 cohort, and the Berry and Lewinsohn post-1950 cohorts, respectively. The estimates from the three cohorts differ by an approximate factor of three. This may be indicative of some of the methodological differences among the studies. For example, it is possible that the estimates made from Berry and Lewinsohn's data may be underestimates. The maximum duration of follow-up in that study was 23 years, with an average follow-up of 16 years. Observations from Finkelstein's data (his Table 1) demonstrate that only 41% (23/56 cases) of total incidence was experienced in the first 24 years since first exposure. That is, 59% of the asbestosis incidence was not expressed until at least 25 years from onset of exposure. Thus, it is likely that the low incidence rates in the Berry and Lewinsohn studies (and, therefore the low estimates of risk predicted from these data) are reflective of the short follow-up period for this group of workers.

On the other hand, Finkelstein's (1982) observations may overstate the incidence of asbestosis because at autopsy there was histologic evidence of silicosis as well as asbestosis in many men. Finkelstein states that "we have, nevertheless, chosen to call their disease 'asbestosis' as we believe that is the pathologic process of most significance. Most of the parenchymal radiographic abnormalities were small irregular opacities and the mortality pattern among the men was consistent with the toxic effects of asbestos" [Ex. 84–44, p. 500].

More importantly, it is indeed possible that all of these investigators may have understated asbestosis risk by examining only certified disability from asbestosis, which is an advanced stage of the disease. As noted in the November proposal, there was evidence of the early signs of asbestosis at levels