

$$R_L/R_0 - 1 = K_L \times f d_{1-10}$$

(Eq. 2)

showing, on the left-hand side, the excess relative risk (excess SMR) as a function of K_L and total dose (fibers times years). It is this form of the equation that is used to derive the individual K_L 's for each of the eight studies. These eight K_L 's are used to derive one overall K_L for lung cancer. Then the excess risk is computed for each five-year age interval; the overall lung cancer risk is then computed as the sum of the risks in each of the five-year intervals from age 25 to age 70. The excess risk is expressed as the number of additional lung cancer deaths per 1000 workers exposed for a specific time period.

Evidence of the linear dose-response relationship for lung cancer is found in several well-conducted epidemiologic studies that examined lung cancer mortality in relation to cumulative asbestos exposure in the workplace (for example, Henderson and Enterline, 1979, Ex. 84-48; Liddell et al., 1977 Ex. 84-59, and Dement et al., 1982, Ex. 84-35). In the three studies cited above, workplace asbestos air concentrations were available from measurements made in the worksite studied. Although the studies differ in the magnitude of the risk found (discussed later in this section), all three demonstrate a linear relationship over the entire range of observation.

As stated in the November proposal, other scientific and scientific groups who have attempted to estimate risk from asbestos exposure have used the linear model for lung cancer [Crump, Ex. 85-22, British Advisory Committee on Asbestos, Ex. 84-216, Acheson and Gardner, Ex. 84-243, Selikoff, Ex. 82-2, EPA, Ex. 84-180, CHAP, Ex. 84-256, National Research Council/National Academy of Sciences, Ex. 321]. The model is generally accepted and OSHA believes use of the linear model for predicting lung cancer due to asbestos exposure is reasonable, and well-supported. Although participants in the rulemaking pointed to the uncertainty associated with the use of the linear model, no one suggested another model for computing the lung cancer risks.

Dr. Hans Weill elaborated on this point:

... As regards the shape of the dose-response slope, and operational judgment is based on the conclusion that there is currently no available evidence that convincingly proves that the slope is not linear, crossing the [excess] risk axis at the origin. This assumption (as made in the OSHA risk analysis) is justified from the observations at moderate and high levels of exposure that generally indicate linearity,

which when extended downward to levels of exposure below which observations are available, are not inconsistent with linear low dose extrapolation [Ex. 99, p. 13].

And, in his testimony, Dr. Weill concluded:

Now, as far as the shape of the curve for the important malignant consequences of asbestos exposure, I think we are all in agreement so far today, that the evidence does not permit us, nor does concern of public health or prudence permit us for the conditions that we are concerned about, to develop on any basis other than linearity of exposure and response in a no threshold model [Tr. 8/19, p. 154].

Dr. William Nicholson of the Mount Sinai Environmental Sciences Laboratory elaborated on the rationale for the choice of the linear model for lung cancer:

In three studies in which it [the linear dose-response curve] has been demonstrated [see above Exs. 84-48, 84-59, and 84-35] the range of exposures is large, over a tenfold range of exposures, that linearity has been documented over a tenfold range of dose. Further, it has biologic plausibility [Tr. 8/19, p. 75].

This biologic plausibility was also discussed by Dr. Kenny Crump, testifying on behalf of the AIA/NA:

There is a theoretical argument [Crump et al., 1978] that suggests that cancer incidence should vary approximately linearly with dose for low doses particularly when there is an appreciable background of carcinogenesis in unexposed populations. . . . If asbestos induces cancer through the same mechanism as smoking, then there is reason to believe that the response should be approximately linear at low dose . . . just as assumed in the OSHA model [Ex. 237A, pp. 8, 25].

Though Dr. Crump noted in his testimony that the linear model for lung cancer "is a hypothesis which is by no means proven" [Tr. 7/9, p. 90], he stated during cross-examination that "all of the estimates I have made in the testimony were based upon a linear model for lung cancer" and that the linear model for asbestos and lung cancer "has been widely used" [Tr. 7/9, p. 118].

Thus, OSHA feels confident in its adoption of a linear model to predict the risk of lung cancer from asbestos exposure. The model has wide support because of its scientific plausibility and reasonableness and its prudence for use in public health decision-making.

B. Data Used in the Calculation of Individual k_L 's. In the November proposal [48 FR 51125], an estimate of lung cancer potency (K_L) was calculated for each of 11 studies using equation 1. For studies with individual exposure data, K_L was the slope of the regression equation fit to these points; for studies having only an overall risk estimate and

average estimate of exposure, this single point was used in the calculation of K_L . For each study, the best estimate of K_L is indicated along with a range of uncertainty. The ranges given are the result of uncertainties in estimates of exposure, methodological uncertainties that led to alternate evaluations of risk or exposure, or, in some cases, statistical uncertainties associated with the use of small numbers.

The differences in the K_L 's among the various studies result from a number of different factors. There do appear to be actual differences in risk depending upon the nature of the asbestos exposure. One potential explanation is that workplaces differ with regard to fiber size distribution (long finer fibers appear to have greater carcinogenic potential than coarse fibers). For example, as several participants in the rulemaking acknowledged, there appears to be a distinct difference in the risk from mining and milling and other processes. As Dr. Nicholson summarized:

I think I stated this morning . . . the possibility that the mining work environment may demonstrate a different pre-unit risk. That is, there's three studies showing somewhat lower risks. At least two of them show, with fairly substantial data, lower risk, that that [lower risk] may be a function of the fiber size distribution in the mining environment.

One may have a much greater number percentage, of long curly fibers, which are readily counted, but are not inspired. And, thus, the fiber counts are proportionately high in that environment relative to the amount of asbestos inspired. It seems to be consistently so for chrysotile and also for amosite. For example, one finds very few cases of mesothelioma associated with amosite mining but a considerable number associated with amosite manufacturing.

And so there is perhaps a difference in the mining environment, where they are working with different type of fiber composition [Tr. 6/19, p. 127].

Thus, where airborne fibers are relatively coarse, the K_L 's are lower than the K_L values found in studies of textile operations where fibers are fine.

Differences may also be explained by variations in study design and other factors influencing the ability to define the dose-response relationships. One of these is the limited knowledge of past fiber exposures of those populations whose mortality was later evaluated. Prior to 1970, few measurements were made in facilities using asbestos fibers. Further, those measurements that were done usually quantified all dust present in the workplace air and not just fibers. Current techniques, which involve use of membrane filters and phase contrast