proposal, suggested several other reasonable methods for producing "medium estimates." In addition to approaches taken by OSHA, Dr. Schneiderman suggested that one look only at the four studies (from the proposal) which also had data on mesothelioma (Selikoff et al., Seidman et al., Peto, and Finkelstein). This selection produced an overall estimate of $K_L$ derived from the individual $K_L$ values of approximately 0.028. He also noted the $K_L$ of 0.020 which results from use of the five U.S. studies only (Selikoff et al., Seidman et al., Henderson and Enterline, Weill et al., and Dement et al. proposed values of $K_L$, Ex. 116, p. 7).

Schneiderman concluded that:

The selection of the value of 0.01 (by OSHA) is based both on the various averages that could be computed and also on the informal or subjective weights given to each of the studies by OSHA. If this value is in error, it is possibly biased *downward* by the inclusion of the miners and millers and the foreign studies. However, any error introduced by an underestimate or $K_L$ will be relatively small. Because of the changing patterns of cigarette smoking which should soon lead to reduced lung cancer mortality among younger (working-age) men, an underestimate of $K_L$ is likely to compensate for possible overestimate of lung cancer mortality in the future [Ex. 116, p., 7–8].

Other possibilities for the calculation of $K_L$ include: (1) Using studies with concurrent exposure data only (Henderson and Enterline, McDonald et al., Peto, and Dement et al.), which gives estimates of $K_L$ of 0.014 (arithmetic mean) or 0.006 (geometric mean); (2) using only the upper limits of the uncertainity ranges, which gives a $K_L$ of 0.059 (arithmetic mean) or 0.02 (geometric mean).

The value of 0.01 falls well within the range of $K_L$'s suggested by participants in the rulemaking. It is less than two times larger than the lowest value suggested for $K_L$ (by Crump). In addition, as OSHA discussed in the proposal, there is a range of uncertainty associated with this value that more than covers all suggested values of $K_L$. Thus, OSHA believes the value of 0.01 to be a valid, reasonable estimate of $K_L$ and has employed it in developing its estimates of risk to support these revised rules.

## II. Estimates of Risk for Mesothelioma

A. *The Model.* For the November proposal, OSHA chose an absolute risk model to predict the risk for mesothelioma from exposure to asbestos. Absolute risk is calculated as observed deaths divided by the number of person-years at risk. It is believed that use of SMR's or relative risk is not appropriate for mesothelioma because the expected number of deaths in a cohort would be close to zero due to the rarity of the disease. The use of absolute risk to predict risk of mesothelioma was not questioned by any participant in the hearing.

In addition to using absolute risk rather that relative risk, this model is different from that used for lung cancer because both duration of time since initial exposure and duration of exposure are determinative or risk. The magnitude of the risk increases linearly with intensity of exposure, whereas the risk increases exponentially with duration of exposure and time from onset of exposure. The rationale for such a model describing mesothelioma risk has been discussed by several authors [Armitage and Doll, 1969, Ex. 84–252; Pike, 1966, Ex. 84–385]. Such a model was utilized by Newhouse and Berry [1976, Ex. 84–342] in predicting mesothelioma mortality among a cohort of factory workers in England. Limited data from three studies are also available on the dose-response relationship for mesothelioma [Seidman et al., 1979, Ex. 84–87; Hobbs et al., 1980, Ex. 132, and Jones et al., 1980, Ex. 84–138].

The model used by OSHA to assess the risk and derive the potency factor for mesothelioma, $K_M$, is given by the following equations:

$AR_M = fxK_M[(t-10)^3-(t-10-d)^3]$
for $t>10+d$

$AR_M = fxK_M(t-10)^3$
for $10+d>t>10$

$AR_M = 0$
for $10>t$

where $AR_M$ is the excess mortality from mesothelioma, f is the intensity of exposure in fibers/cc, d is the duration of exposure in years, t is time after first exposure in years, and $K_M$ is the proportionality constant that is a measure of the mesothelioma carcinogenic potency (slope of the dose-response curve) [Ex. 84–392].

Dr. Marvin Schneiderman discussed several aspects of the choice of this model for assessing mesothelioma risks. In his written testimony he stated:

The formula for estimating mesothelioma risk has a somewhat different form [from that of lung cancer]—in keeping with the fact that the excess risk from mesothelioma is measured as an "absolute" rather than a "proportional" risk. . . .

What these formulas say is, first, no disease will be seen sooner that 10 years after first exposure (induction period effect). Second, if d is relatively short (compared to t) then there will be less disease than if the duration of exposure is long. Finally, the age-at-first exposure effect is subsumed in the exponent 3.

The Consumer Product Safety Commission, in the report mentioned above [Ex. 84–256], also gives this formula. The NRC/NAS report on asbestiform fibers [Ex. 321] notes the great sensitivity of the estimate to the exponent of the (t–10) [and the (t–10–d)] term. Taking the term $(t-10)^3$ as a base, if t=40, the relative values of the term raised to different exponents are:

| | | |
|---|---|---|
| *NRC/NAS "middle"* | :$(t-10)^{3.2}$ | $1.97\times(t-10)^3$ |
| Peto, et al. | :$(t-10)^{3.5}$ | $5.48\times(t-10)^3$ |
| Nicholson | :$(t-10)^4$ | $30.0\times(t-10)^3$ |

These values are somewhat different if the "delay" term is neglected [Ex. 116, p. 6–7].

In his written testimony, Dr. Crump raised several issues concerning the choice of this expression for the time factor. He stated:

Most studies of mesothelioma predict that the mortality risks are a power of elapsed time since first exposure, as assumed by the OSHA model. However, we cannot be sure that this steep rate of increase extends indefinitely into old age as assumed by OSHA. In the Selikoff cohort, which contains the best information on mesothelioma mortality in old age, the number of *mesotheliomas in the oldest group* (55+ years since first exposure) is only about ½ the number predicted from the OSHA model. Although some of this shortfall may be due to underreporting in old age, it is also possible that the deficit is real. If so, the OSHA model will overestimate risk at oldest ages. None of the cohorts contain information on mesothelioma risk after 30 years past termination of exposure. OSHA's assumption that the risk will continue to increase represents an assumption which is not presently verifiable [Ex. 237A, p. 34].

In a post-hearing comment, Dr. Crump extended his argument. In addition to the data from the Selikoff cohort discussed above, Dr. Crump also discussed the mesothelioma data from the recently completed follow-up of the Seidman et al. study of amosite workers. He pointed out that for these data, ". . . the mesothelioma rate did not continue to raise with increasing age from first exposure, but dropped off 35–40 years from first exposure to 1.8/1000 person-years, which is about ⅓ of the rate observed for 30–35 years from first exposure" [Ex. 312a, Vol. I, Tab A, p. 7]. Dr. Crump noted that, although the OSHA model assumes "that the mesothelioma mortality rate increases indefinitely as a power of time from first exposure . . . the multistage model does predict an eventual reduction, the timing of which is determined by the number of stages affected and the rate of elimination of fibers from the body" [Ex. 312a, p. 8]. Dr. Crump went on to conclude that "if the reduction is real, then the OSHA model will provide a considerable overestimate of

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