Mesothelioma Model

The absolute risk model adopted for mesothelioma in the EPA 1986 update is a particular adaptation of the multistage model for carcinogenesis, which predicts that incidence is independent of age at first exposure and increases as a power of time since first exposure (Armitage and Doll, 1961; Pike, 1966; Cook et al., 1969; Peto et al., 1982). The model adopted in the EPA update was based on evidence of the time course of the mortality rate in several cohorts. This model can be derived by assuming that the mortality rate at time t after the beginning of exposure is the sum of the contributions from exposure at each increment of time, du, in the past. The contribution to the mortality rate at time t from exposure to $E(u)$ fibers (f)/ml (as measured by PCM) at time u is assumed to be proportional to the product of the exposure rate, $E(u)$, and $(t-u-10)^2$, the square of the elapsed time minus a lag of 10 years. Thus, as with the lung cancer model [Eq. (2)], the mesothelioma model assumes a 10-year lag before exposure has any effect upon risk. With the additional assumption that the background rate of mesothelioma is zero, the mesothelioma mortality rate at time t after the beginning of exposure is given by

$$I_{\mathrm{M}}(t) = 3 \times K_{\mathrm{M}} \times \int_0^{t-10} E(u) \times (t-u-10)^2 \, du \quad [3]$$

where t and u are in years, and $I_{\mathrm{M}}(t)$ is the mortality rate per year at year $t$after the beginning of exposure. (The factor of "3" is needed to retain the same meaning of the mesothelioma potency factor, K_{M}, as defined in the EPA 1986 update.)

If exposure is at a constant intensity, E, for a fixed duration, D, beginning at $t = 0$, this model can be written in the form presented in the EPA 1986 update:

$$I_M(t) = \begin{cases} 0 & 0 \le t < 10 \\ K_{\mathrm{M}} \times E \times (t-10)^3 & 10 \le t < 10+D \\ K_{\mathrm{M}} \times E \times [(t-10)^3 - (t-10-D)^3] & 10+D \le t \end{cases} \quad [4]$$

This model predicts that the mesothelioma mortality rate varies linearly with exposure intensity E (for fixed duration, D, and time since first exposure, t). Upon rewriting the model in the