Further extensions of the risk assessment model

Fiber chemistry is an important determinant of breakage and solubility in tissues, and hence of clearance. Tissue burden and, therefore, fiber carcinogenicity are clearly affected by the composition of the fiber. Moolgavkar and coworkers (2000, 2001) extended the methods used in their assessment of RCF to investigate whether chemical composition of fibers has a role beyond determining biopersistence. Using available data from a number of long-term oncogenicity inhalation experiments, they showed that the results were consistent with the hypothesis that the oncogenic potential of long man-made vitreous fibers is determined mainly by their biopersistence. In other words, the data analyzed were shown to be consistent with the view that "a fiber is a fiber." The carcinogenic potential is determined by the lung burden of fibers which, in turn, is determined by biopersistence. That is, the authors showed that fiber chemistry influences fiber carcinogenesis primarily through its role in determining biopersistence. A direct mechanistic role, if any, of chemistry in fiber carcinogenesis is of secondary importance. These conclusions allowed the authors to estimate a common potency factor describing the oncogenic potential for all MMVFs.

Turim and Brown (2003) extended these results and considered various means of extrapolating human equivalency concentrations from animal test results. They showed that of all the models considered, including benchmark dose and other statistical models, the weight of evidence argues in favor of the MVK two-stage clonal expansion model for the following reasons:

- The MVK model explicitly takes into account the temporal distribution of the pattern of lung burden. Other models consider only the steady-state level of fibers in the lung.
- It is the only model that explicitly incorporates time-dependent doses.
- By simulating the initiation and promotion activities that are known to underlie cancer induction the model rests on a biologically significant and generally accepted theory of carcinogenesis. Other models rely on purely statistical techniques.
- The MVK model provides a better fit of the observed laboratory data than the other models, taking into account the number of parameters that are used in the model.
- The model is consistent with the results of a number of experiments conducted with synthetic vitreous fibers and was able to detect the effect of overload at high exposure concentrations.
- It is the only model that can be subjected to an external validity check because the parameters estimated in the model must be biologically plausible.

Risk from exposure to RCF

Turim and Brown (2003) summarized the results of the previous investigations in estimating cancer risk. They found that the 95% upper bound risk of excess lifetime lung cancer risk to a non-smoking workforce is:

- 3×10^{-5} for an exposure of 1 f/cc
- 1.5×10^{-5} for an exposure of 0.5 f/cc
- 0.3×10^{-5} for an exposure of 0.1 f/cc

For an occupational workforce with typical smoking habits, the corresponding 95% upper bound excess lifetime risks are approximately three times higher.

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