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EDITORIAL

Uncertainty Factors in Noncancer Risk Assessment

The science behind uncertainty factors in noncancer risk assessment has progressed considerably beyond the use of standard default values of 10. Why? Increased knowledge of toxicokinetics, toxicodynamics, mechanisms of toxicity, and temporal aspects of critical effect has emerged for many chemicals. Moreover, risk assessment scientists are making more detailed evaluations to support the use of uncertainty factors based on the available data.

Several reports exist on the scientific underpinnings of uncertainty factors (McColl, 1990; Kroes *et al.*, 1993; HERA, 1995). Dourson *et al.* (1996) also highlight available data for each of several areas of scientific uncertainty and provide examples from U.S. Environmental Protection Agency and Health Canada in which data have been used to support the selection of uncertainty factors values other than default.

Despite widespread use in noncancer risk assessment over a number of years and by numerous health agencies, uncertainty factors have only occasionally had such focused reviews. Many of the underlying assumptions and choices of uncertainty factors in noncancer risk assessment are similar among these health agencies. Such similarity could be one foundation of global harmonization of risk assessment methods, a formidable task undertaken by the International Programme on Chemical Safety (Sonich-Mullin, 1995).

Uncertainty factors are not precise. The underlying data that support these factors demonstrate large variability. However, the incorporation of all available scientific data into the risk assessment process fosters increased research and ultimately reduces uncertainty. This, in turn, supports the use of data-derived uncertainty factors, resulting in noncancer risk assessments in which greater confidence can be placed. Examples in which research has reduced the use of default factors are readily found (e.g., Jarabek, 1994).

Finally, ongoing discussions on the underlying basis for uncertainty factors in noncancer risk assessment become more relevant to similar assessments done for cancer endpoints. Witness the U.S. EPA's proposed revisions to the 1986 cancer risk assessment guidelines (EPA, 1996) that advocate the use of a margin-of-exposure approach for carcinogens for which evidence exists of a nonlinear dose–response relationship. This method is similar to that which is already in use by Health Canada (Meek *et al.*, 1994), for example. Clearly, a margin-of-exposure approach will necessitate the use of uncertainty factors, or a similar construct. Thus, research into the underlying basis of these factors may have double benefits.

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