

with which extrapolation to the human exposure situation is carried out. Furthermore, such results can have an important influence on the kinds of additional toxicological or biological studies that might be required to resolve the issue. Thus, it would seem unwise to restrict *a priori* the number of species that should be tested in lethality studies.

Important information can also be obtained from lethality studies performed with different routes of administration. In the past, such observations have had an important bearing on conclusions regarding the relative bioavailability (amount absorbed) of various chemicals following exposure by different routes of administration. They have been essential for determining how chemicals can be handled safely. These data can also help to establish the exposure conditions that are relatively without risk when chemicals are to be used as articles of commerce. Thus, it would be unwise to limit *a priori* the routes of administration that should be employed in lethality studies.

Whether to employ a particular lethality test or not, or the precision one needs if the test is chosen, depends on the anticipated use that will be made of the data generated. This means that one must look at the toxicological questions that are being asked. Estimates of acute lethal potency are presently very important data for the classification of chemicals when these substances are transported as hazardous chemicals. In the case of accidental spills and derailments, for instance, the adverse effects of consequence to humans are those associated with the temporary acute exposure to high concentrations of the chemical. In the occupational setting, accidental discharges may occur, resulting in acute exposures to potentially unsafe amounts. Acquisition of sound LD50 data are essential in such situations.

It is important to point out that there are no known, validated alternatives to the use of animals for the assessment of lethal potency. Nor are such alternatives likely to appear in the near future. Attempts are being made to develop techniques that predict lethal properties of certain classes of chemicals on the basis of already known structure-activity relationships. Quantitative Structure-Activity Relationships (QSAR) and Quantitative Structure-Toxicity Relationships (QSTR) are examples of such approaches. The reliability of the QSAR approach depends on the availability of data reflecting (1) well-defined interactions between chemical substances (2) belonging to congeneric series of structures and (3) an already known active site in a biological system. The application of the QSAR approach is said to presuppose the presence of an active site coupled with unambiguity (in terms of mechanism of action) of the observed biological effects. The present state of toxicological knowledge is far from providing the necessary data that could make use of the QSAR approach. Thus, while these efforts are to be encouraged, it is evident that they will not be reliable substitutes for experiments in laboratory animals.

There is an important political issue that also bears on the safety evaluation process. Toxicological assessments are used to protect the public from the potentially adverse effects of chemicals. Public perception is that individuals have the right to live in a so-called "safe" environment. The adversarial-litigation climate that reigns in North America reflects this public perception. This climate indirectly influences the practice of toxicology. What toxicologist or government regulator is likely to decide in favor of not performing a particular toxicological study, thought to be of limited value, when court litigation at some later date for this decision remains a possibility?