Guide for uniform carcinogen regulations issued

The White House Office of Science & Technology Policy has issued its formal report on chemical carcinogens. Termed a review of the science and its associated principles, the document is the result of a two-year effort by 20 senior scientists from nine federal health-related agencies to reach an agreement upon scientific principles to guide federal agencies in assessing cancer-causing risks from chemicals.

Its overall purpose is to provide a framework for achieving greater consistency and continuity within and among agencies in how they regulate chemical carcinogens. Over the years Congress has enacted more than 20 laws, some amended several times, establishing programs to deal with hazardous substances. As the report notes, these laws are not uniform in their view of disease, the role chemical substances might play in its incidence, and what ought to be done about potential toxic substances and carcinogens.

Consequently, each agency has developed its own guidelines for assessing the risks posed by chemicals. These guidelines have sometimes been contradictory, leading to confusion over how the government might act in any specific situation. That situation may well change now.

The report consists of two parts. The first part lays out the general principles, 31 in all, that can be used by regulatory agencies as they review their own specific guidelines for performing cancer risk assessment. The second part is divided into six chapters assessing the current state-of-the-science concerning carcinogenesis and cancer risk assessment. Taken together, these parts provide "a powerful tool to help achieve balance and objectivity in the complex process of regulating man-made and naturally occurring chemicals that may cause cancer," says OSTP director George A. Keyworth II.

The OSTP document is certainly more flexible and contains many more caveats than other carcinogen policy statements issued by federal agencies over the years. A case in point is the Occupational Safety & Health Administration's generic proposal on regulating workplace carcinogens issued in late 1977.

C&EN staff photo

Keyworth: help achieve balance

Under its proposal, OSHA would have considered as a known human carcinogen any substance whose carcinogenicity had been determined in humans; or in two or more mammalian species of test animals; or in one species, if the results of the study had been replicated; or if positive results in one mammalian species were supported by positive results of short-term tests.

In reaching a decision, OSHA said it would place as much weight on experiments in which only benign tumors were observed as upon experiments in which both malignant and benign tumors were introduced. Results showing an increased incidence of tumors in treated animals would be regarded as positive evidence of carcinogenicity regardless of spontaneous tumor incidence, provided the increase was statistically significant. A finding that a substance was carcinogenic would have triggered immediate, stringent regulation to reduce worker exposure to it, no matter how extensive the exposure actually was.

In its discussion on interpreting the results of long-term tests, the OSTP report says that the term carcinogen should be used in a broad sense, meaning a substance that is capable under appropriate test conditions of increasing the number of neoplasms (combining benign and malignant when scientifically defensible) or decreasing the time it takes them to develop. At this point a draft of the OSTP report, issued in May 1984, says that "agents found carcinogenic in animal studies [subject to certain considerations] are considered suspect human carcinogens."

However, that sentence is omitted in the final report. It now says, "Careful consideration to relevant issues (cited in another part of the report) should be given prior to a determination that a chemical is an animal carcinogen.

"Deference should be given to the International Agency for Research on Cancer principle: 'that in the absence of adequate data in humans, it is reasonable, for practical purposes, to regard chemicals for which there is sufficient evidence of carcinogenicity in animals as if they presented a carcinogenic risk to humans.'

"However, this presumption is evaluated along with other relevant information in making a final judgment concerning human carcinogenicity and should not foreclose further inquiry into the human relevance of animal carcinogens."

The OSTP report goes on to note that some experimental animal models ordinarily have high incidences of certain tumors, posing special problems in evaluating tumor data from these test animals. It says that, for any animal study, confidence is increased when the incidence of tumors is elevated markedly in the treated groups compared to controls; tumor incidence is significantly increased at multiple anatomical sites; and tumor latency is significantly reduced. Confidence is also increased by evidence of a dose-response relationship, whereas lack of such evidence may reduce the likelihood that the effect is associated with the treatment.

The final report was published in the March 14 issue of the *Federal Register*. Copies of "Chemical Carcinogens: A Review of the Science and Its Associated Principles" may be ordered from the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402, telephone (202) 783-3238. □