Dispute over Cancer Risk Quantification

Supreme Court will review appeals court ruling requiring risk analysis in support of OSHA's proposed benzene standard

The Occupational Health and Safety Administration (OSHA), more than other regulatory agencies, has resisted the idea that rule-making to limit human exposure to carcinogens should rest in part on the admittedly immature, if not primitive, art of risk quantification. Furthermore, appeals courts in three federal circuits have gone along with OSHA in this matter by upholding its rules that sharply reduce allowable exposure to asbestos dust, vinyl chloride, and coke oven emissions. But last October OSHA's cancer policy, which in some important respects is still emerging, suffered a blow when the Fifth Circuit Court of Appeals in New Orleans rejected the agency's so-called "half-billion dollar" rule on benzene exposure because no cost-benefit data had been presented to justify it.

On 21 February, the Supreme Court agreed to review the benzene ruling. It is expected to hear the case next fall, with its own decision to come a year from now. If the decision should go against OSHA, the agency will have to begin trying to support its rule-making on benzene and other carcinogens with risk quantification studies of the kind that it now regards as meaningless and often misleading. Also, with such an adverse ruling, OSHA might find that its current proposal to simplify and expedite rule-making by establishing generic standards for regulating carcinogens has been largely undermined.

"The importance of the benzene case [to the OSHA cancer policy] cannot be understated," says Margaret Semario, an industrial hygienist with the Industrial Union Department of the AFL-CIO, which has intervened in the case on the side of OSHA.

The dour view which OSHA takes of risk quantification for carcinogens is not shared by the Environmental Protection Agency's cancer assessment group, which is chaired by Roy E. Albert, professor of environmental medicine at New York University. In fact, OSHA is said to have been the only agency taking a hard and fast line against risk quantification (at least for carcinogens in the workplace) during the deliberations last year of the Interagency Regulatory Liaison Group's risk assessment panel.

This panel's recent report *Scientific Bases for Identifying Potential Carcinogens and Estimating Their Risks* says that available quantification methodologies "permit, to the extent currently possible, a crude order-of-magnitude, estimate of risk. . . ." According to Albert, an earlier draft of the report showed a "strong OSHA slant" and "aversion to quantification." But the final wording, he indicated, sanctions the kind of cancer risk quantification EPA has been doing, and is required to do by some of the laws it administers, for carcinogens in the general environment.

By its proposed ruling on benzene, OSHA would reduce workplace exposure to this widely used hydrocarbon compound from 10 parts per million, the standard set in 1971 as a safeguard against noncarcinogenic health effects, to 1 ppm, regarded by the agency as the lowest standard achievable. The justification for the new standard lies principally in the fact that several epidemiological studies conducted during the 1970's have shown benzene to be a leukemogen.

The investigation on which OSHA has principally relied was made by Peter Infante of the National Institute of Occupational Safety and Health. Infante found that the cohort of 748 workers exposed to benzene in two Goodyear Company plants in Ohio between 1940 and 1949 suffered nine deaths from leukemia, an incidence of mortality from this disease seven times greater than that observed either in the general population or in the cohort of workers who had not been exposed to benzene. The levels of exposure experienced by the Goodyear workers are much in dispute but the court concluded that "exposure was probably around 100 ppm for most of the period studied with occasional exposure levels as high as several hundred parts per million." In any event, the exposure was greater than that which is permissible now.

Benzene is employed in numerous industrial processes, but most of it is used in the chemical, tire-manufacturing, and petroleum industries (gasoline contains up to 2 percent benzene). Altogether, some 629,000 workers are said to be exposed to benzene. According to OSHA estimates, the cost to industry of complying with the 1 ppm standard would total about $500 million, a large sum even though it is but half what industry says the cost would be.

The industry attack on the proposed benzene standard, which has been led by the American Petroleum Institute (API), has been based in part on the contention that there is a no-effect exposure threshold for benzene which lies comfortably above the existing 10 ppm standard. But the Fifth Circuit Court rejected that argument and ruled in favor of the API solely for the reason that a cost-benefit assessment to support the standard was lacking. (The court also set aside a proposed OSHA rule to require the use of protective clothing to prevent all dermal contact with benzene, doing so on the grounds that radioactive benzene had not been used—as the most up-to-date research tool available—to get a definitive answer to the question of whether the compound can be absorbed through the skin.)

The circuit court gave great weight to the fact that the Occupational Safety and Health Act of 1970 says that standards promulgated under it must be "reasonably necessary and appropriate." This language had not figured importantly in OSHA's earlier rule-making, for in promulgating other exposure limits (such as the one on vinyl chloride) it had looked to the part of the statute which says that the agency "shall set the standard which most adequately assures, to the extent feasible, on the basis of the best available evidence, that *no employee* [emphasis supplied] will suffer material impairment of health. . . .")

The court observed:

> We are not persuaded by OSHA's argument that this standard should be upheld since the lack of knowledge concerning the effects of exposure to benzene at low levels makes an estimate of benefits expected from reducing the permissible exposure level impossible. The statute requires all conditions imposed by a standard to be reasonably necessary to provide safe or healthful employment, and it requires decisions to be based on the "best available evidence," "research, demonstrations, experiments, and such other information as may be appropriate," "the latest scientific data in the field," and "experience gained under this and other health and safety laws." By requiring the consideration of such kinds of information, Congress provided that

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OSHA regulate on the basis of knowledge rather than on the unknown. . . .

This does not mean that OSHA must wait until deaths occur as a result of exposure at levels below 10 ppm before it may validly promulgate a standard reducing the permissible exposure limit. . . . nevertheless, OSHA must have some factual basis for an estimate of expected benefits before it can determine that a one-half billion dollar standard is reasonably necessary. For example, when studies of the effects of human exposure to benzene at higher concentration levels in the past are sufficient to enable a dose-response curve to be charted that can reasonably be projected to the lower exposure levels, or when studies of the effects of animal exposure to benzene are sufficient to make projections of the risks involved with exposure at low levels, then OSHA will be able to make rough but educated estimates of the extent of benefits expected [from the more stringent standard]. . . .

In a brief filed with the Supreme Court, the Secretary of Labor, speaking for OSHA, took strong exception to the Fifth Circuit's view of the matter, asserting:

. . . [T]he court of appeals overestimated the precision available in scientific studies of risk from exposure to carcinogens. There are a number of obstacles that make the measurement of benefits difficult. For example, it is difficult to study the development of cancer in groups of persons because it is not known how much of a given substance they may have been exposed to in the past; moreover, persons may have been exposed to several different causes of cancer, and it is difficult to isolate the effects of each. There may be a substantial lag between initial exposure to a carcinogen and the development of the disease; this makes it difficult to know when any sample of persons has developed all of the cases of cancer that may fairly be attributable to a particular substance. . . . In other words, the Secretary believes that it is not possible to conclude, with any precision, how many cases of cancer could be avoided by reducing exposure from 10 ppm to 1 ppm. . . .

Observing that the circuit court had referred to an EPA study "A preliminary report on population risk to ambient benzene exposure" as evidence that risk quantification is possible, the secretary noted that the EPA report said that exposure of the whole population to levels even as low as one part per billion for only 24 hours would cause between 30 and 80 cases of leukemia yearly. EPA conceded, the secretary said, that its estimates were "devised by very crude methods and could be in error by several orders of magnitude, so that it could confidently conclude only that one sort of exposure would cause between 0.3 and 8000 deaths yearly." Such estimates, the secretary added, are not "sufficiently precise for use in setting occupational health standards."

As the above suggests, OSHA's differences with EPA over risk quantification seem nearly as great as those it has with the Fifth Circuit Court. In an interview with *Science*, Albert indicated that, in his opinion, a linear nonthreshold dose-response model can be made for benzene that would be useful for regulatory purposes. "I wouldn't say that the whole decision should be based on it," Albert said. "But I think it's like the ostrich putting its head in the sand not to do it."

A number of environmental and health and safety statutes, such as the Toxic Substances Control Act, the pesticide act, and the Consumer Product Safety Act, explicitly call for a balancing of risks and benefits, and some other laws contain language which might be interpreted as requiring it.

Although the circuit court left some latitude as to how precise the quantification should be, it clearly called on OSHA to strike a positive balance in justification of its proposed standards, which could amount to adding up potential cancer deaths and putting a dollar figure on each one. This might open up a rich new mother lode of political wrangling and legal disputation that could extend to the interpretation, or reinterpretation, of other statutes besides the Occupational Health and Safety Act.

Certainly in the case of occupational exposure standards, industry groups such as the API are not likely ever to see eye to eye with OSHA and the AFL-CIO on the value to put on lives that may be shortened because of exposure to carcinogens in the workplace. Anyway you look at it, the Supreme Court's ruling in the benzene case could turn out to be one of the landmarks in the evolution of a national cancer policy.

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EPA Risk Assessment Policy

The rationale for the Environmental Protection Agency's policy for assessing cancer risk was set forth in the May 1977 issue of the Journal of the National Cancer Institute *in an article by Roy E. Albert, chairman of the EPA Cancer Assessment Group (CAG), Elizabeth Anderson (executive director of the CAG), and Russell E. Train, then EPA administrator. The following was extracted from that article.*

The first important regulatory step against chemical carcinogens in the United States was the Delaney Clause of the Pure Food and Drug Act that set a zero tolerance limit for carcinogenic food additives. However, the general application of such an idealized form of regulatory action is unrealistic because many carcinogens are too important to eliminate completely without unacceptable socioeconomic consequences. Consonant with this view, several of the EPA's enabling laws, particularly FIFRA and TOSCA, require the evaluation of risks and benefits as the basis for regulatory decisions . . . .

The quantitative assessment of the impact of a suspect carcinogen on cancer induction in humans at unregulated levels of exposure is useful for judging the need for regulatory action. Of the half dozen instances in which quantitative comparisons can be made between animals and humans, the magnitude of carcinogenic response in the most sensitive animals tested does show a reasonable comparability to that of humans. However, substantial differences occur in sensitivity, even among different strains in the same species of test animals. Thus regulators must evaluate cross-comparisons between animals and humans with reservations.

Another aspect of the quantitative risk assessment involves extrapolation of dose-response relationships from high to low levels of exposure. All the instances that we have of cancer induction in humans and animals by known chemical and physical agents involved large exposures, compared with those that concern the setting of exposure standards. Estimates, therefore, are required for the level of cancer risk at exposures far below those for which observable responses have been obtained. To make such extrapolations, some shape to the dose-response curve must be assumed. For this purpose, it is probably most appropriate to assume a linear nonthreshold dose-response relationship to estimate the maximum response. This linear pattern of response has been observed in humans who were exposed to certain forms of ionizing radiation and who developed lung cancer as a result of cigarette smoking. It is also the pattern of response observed for the induction of genetic mutations; possibly genetic damage is the fundamental derangement in cancer cells. The linear nonthreshold dose-response relationship is conservative in predicting the largest response for any given level of low-dose exposure. Such a dose-response pattern implies that a safe level of exposure is nonexistent. However, the use of several extrapolation models is appropriate to convey the range of uncertainty in these estimates.