



Risk in Perspective

The legacy of one in a million

"No magic risk number can substitute for informed and thoughtful consideration by accountable officials who work with the public to make balanced decisions."

Public officials shoulder the responsibility of determining which involuntary threats to human health are unacceptable and which are acceptable. For example, how much exposure to a cancer-causing chemical, if any, should be regarded as acceptable for regulatory purposes? In this issue of RISK IN PERSPECTIVE, we offer a historical perspective on this question as well as some principles that should govern future decisions.

The Demise of the "Safe" Dose

Early thinking about acceptable risk was contributed by regulatory toxicologists, who suggested that "safe" levels of human exposure to chemicals could be defined. While virtually all chemicals are toxic at sufficiently high doses, many toxicologists believe in the concept of a "threshold" dose below which no one will be harmed. Laboratory experiments are undertaken to determine the highest level of exposure to a chemical that does not have an adverse effect on test animals. This no-observed-adverse-effect-level (NOAEL) is then divided by a safety factor of 100 or 1,000 to determine the "safe" human dose.

While the concept of a "safe" dose continues to have substantial support today, many scientists believe the concept is not applicable to cancer-causing chemicals. On the basis of radiation biology and epidemiology, it has been hypothesized that any exposure to a cancer-causing chemical is associated with some increase in the probability of tumor formation. If chemicals cause tumors through direct interaction with DNA (so-called "genotoxic carcinogens"), the relationship between dose and response may have no threshold. Although cells can repair damage to DNA, these mechanisms may not always be 100 per cent effective.

Even if carcinogens exhibit threshold doses, the levels may be too small to be helpful to regulators. People are exposed to numerous chemicals from natural and man-made sources, and this

background exposure may exceed whatever threshold exists for a particular cancer-causing mechanism. Moreover, some people may be more susceptible to cancer than others, which means that background levels of exposure may already exceed thresholds for those individuals in the population who are particularly susceptible to cancer. On the basis of these arguments, some scientists emphasize that background levels of exposure to cancer-causing agents are already initiating the carcinogenic process.

De minimis Risk at FDA

The emerging notion of "non-threshold" chemicals challenged regulators at the Food and Drug Administration, who are responsible for guaranteeing the safety of the nation's food supply. How much of a carcinogenic food additive, if any, should be permitted in meat?

During the 1970's, the FDA recognized that some procedure would be necessary to quantify low-dose cancer risks from meat additives and to determine a degree of risk that could be regarded as "essentially zero." FDA rejected detectability as a standard for safety because serious health risks might exist below chemical detection limits and detection technologies were improving rapidly.

FDA's earliest proposal was to use animal data and a probit model to define a "virtually safe dose" that was associated with an incremental lifetime cancer risk of 1 in 100,000,000. Later, FDA replaced the probit model with a linear dose-response model, which was considered more protective than the probit model. When switching to the more protective dose-response model, FDA determined that a risk level of 1 in 1,000,000 would be adequate to protect public health. FDA considered but rejected 1 in 10,000 as an "essentially zero" level of excess cancer risk. Note that if 200 million Americans were each exposed to a meat additive that posed an 1-in-10,000 lifetime risk, 20,000 excess cases of cancer would be predicted over a lifetime. This



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example illustrates that the size of the exposed population, as well as the level of individual risk, need to be considered by public officials.

The federal courts have upheld the authority of regulatory agencies to define *de minimis* levels of risk from exposure to toxic chemicals unless the statute in question compels zero risk. The Delaney Clause, for example, effectively compels the federal government to set zero tolerance levels for any cancer-causing additive that concentrates in food. Agency efforts to permit risks as large as 1 in 1,000,000 from color additives and selected food additives have been overturned by federal courts. Given the impracticality of the zero-risk standard, Congress is now considering legislation to modernize the Delaney Clause.

Significant Risk at OSHA

In the late 1970's the Occupational Safety and Health Administration proposed a generic standard for identifying and regulating chemical carcinogens in the workplace. The proposal called for reduction of all carcinogenic exposures to the lowest levels that are technologically and economically feasible, regardless of the number of workers exposed or the size of the risks to workers. A "carcinogen" was defined as any chemical that has been shown to cause cancer in one sound study of animals or people. Industry petitioners challenged OSHA's emerging policy and argued for both quantitative risk assessment and benefit-cost analysis.

In the 1980 benzene case the Supreme Court held that OSHA must determine that a cancer risk is "significant" before taking steps to reduce or eliminate the risk. Justice John Paul Stevens commented favorably on the developing discipline of quantitative risk assessment. Stevens also opined that a reasonable person might regard a lifetime risk of 1 in 1,000 as significant yet regard a risk of 1 in 1,000,000,000 as trivial. In 1981, Justice William Brennan wrote for a majority of the Court (including Stevens) rejecting the legitimacy of benefit-cost analysis under the Occupational Safety and Health Act. Since these two rulings, OSHA has embraced quantitative risk assessment and used 1 in 1,000 as a threshold of significant risk.

EPA's Range of Acceptable Risks

The creation of the Superfund program in 1980 spawned an explosion of risk assessments at abandoned waste sites across the country. In the Superfund program, excess cancer risk is estimated based on exposure to a hypothetical highly exposed individual living near a hazardous waste site. In the early years of the program, a range of acceptable risk from 1 in 10,000 to 1 in 10,000,000 was used informally by some

Superfund managers. In the 1980's the 1 in 1,000,000 standard became more frequently used as a justification for no-action decisions and, in some circumstances, as a cleanup goal. This number was apparently borrowed from FDA, even though the size of the exposed populations are not comparable and the costs of compliance in the two cases are not comparable. More recently, the Superfund program has defined acceptable excess cancer risk as a range from 1 in 10,000 to 1 in 1,000,000, which provides managers flexibility to consider site-specific factors such as population density, feasibility, and cost-effectiveness.

The range-of-risk approach has also been adopted by other program offices within EPA. In setting guidance for state water quality standards, EPA recommends a range of acceptable risk from 1 in 100,000 to 1 in 10,000,000, although in recent years the agency has approved state plans with an implicit risk level as large as 1 in 10,000. Meanwhile, EPA's air office seeks to reduce risk to as many people as possible to 1 in 1,000,000 while assuring that the maximally exposed individual is protected against risks greater than 1 in 10,000. During deliberations over the 1990 Amendments to the Clean Air Act, Congress rejected a prominent proposal to shut down any industrial facility that could not comply with a cancer risk level of 1 in 10,000 and ultimately 1 in 1,000,000 for the maximally exposed individual. While Congress retained the 1-in-1,000,000 benchmark as a screening tool to guide EPA priorities in setting residual emission standards, Congress expressed a healthy skepticism about the scientific basis of current risk assessment practices. Congress called for a National Academy of Sciences study of EPA's risk assessment methods and a Commission on Risk Assessment and Management to recommend a new legislative framework.

Beyond Magical Risk Levels

Although some observers see value in "bright-line" levels of acceptable risk, history suggests that acceptable risk will ultimately be defined on a case-by-case basis. Key decision factors such as the size of the exposed population, the resource costs of meeting risk targets, and the scientific quality of risk assessments vary enormously from one decision context to another. Administrative discretion is necessary to weigh these factors on a case-by-case basis. No magic risk number can substitute for informed and thoughtful consideration by accountable officials who work with the public to make balanced decisions.

Further Reading

Alon Rosenthal, George M. Gray, and John D. Graham, "Legislating Acceptable Cancer Risk from Exposure to Toxic Chemicals," *Ecology Law Quarterly*, vol. 19, pp. 269-362, 1992.

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