Hazards of risk assessment

Washington

The art of identifying and regulating human health hazards — a ramshackle mix of science, black magic and guesswork, as it is currently practised by the US government — is now moving into the even murkier waters of economics. After years of operating in the grey world of animal models and statistics, officials are beginning to realize that many of their regulations bear little relation to real-world risks. As they attempt to reform the system, they are finding strong arguments for weighing the costs of regulations with their benefits — something that only a decade ago was tantamount to heresy.

Both in regulation and evaluation, "the time is absolutely ripe for re-evaluation", says former FDA commissioner Frank Young, now deputy assistant secretary for health, science and the environment at the Department of Health and Human Services. "We've failed the public in not doing the scientific work of risk assessment." First warning of major changes came last year with a virulent attack on the system from economist Richard Belzer. That an economist would argue for more cost-benefit considerations in risk assessment may not be surprising. But Belzer works for the White House Office of Management and Budget, and his 13-page tirade against current regulatory practices came not in an academic journal, but in the *Regulatory Program of the United States*, the official statement of government policy philosophy.

Belzer minced no words in describing what he saw as a regulatory system crippled by its reliance on flawed assumptions, animal models, and its shortsighted approach to overall risks.

"The continued reliance on conservative (worst case) assumptions distorts risk assessment, yielding estimates that may overstate likely risks by several orders of magnitude", Belzer warned. Such conservatism forces the Federal Government to direct scarce resources "to reduce what are often trivial carcinogenic risks while failing to address more substantial threats to life and health".

As an example of such inequities, Belzer pointed to the banning of EDB, a grain and soil fumigant that combats peanut mould, which can harbour the potent carcinogen aflatoxin B. In part because of the decision to forgo the chemical, the estimated cancer risk from one peanut butter sandwich is now about 75 times that of a full day's dietary exposure to EDB.

Prompted by Belzer's attack on the status quo, the White House Office of Science and Technology Policy set up a panel of representatives from all the regulatory agencies to reconsider the subject. Formed as a subcommittee of the Federal Coordinating Council for Science Engineering and Technology (FCCSET), the panel is charged with ensuring that policies on risk assessment

reflect scientific consensus and are uniformly applied across the government.

That has turned out to be an instructive exercise. One of the first issues to come under FCCSET scrutiny was the process of scaling from animals to humans in determining risk. One regulatory agency, the Food and Drug Administration (FDA), uses a scaling factor based on the difference in body weight between rats and humans. The other major regulatory agency, the Environmental Protection Agency (EPA), scales up on the basis of surface area. On average, the two methods result in estimated risks that are a factor of ten apart.

For 15 years the two agencies have agreed to disagree on the discrepancy, says William Farland, director of EPA's health and environmental assessment office. There were good scientific arguments for both methods, he points out. But the FCCSET committee looked at the same data and came to a different conclusion. Neither method is obviously right, the panel said, so why not find a compromise? It recommended that both agencies adopt a scaling rule based on body weight to the three quarters power.

Because of a paucity of human epidemiological studies and no good way to convert from high animal doses to low human doses, EPA and FDA have been forced to rely on default assumptions and conservative models. As many as 40 assumptions are made in the absence of scientific data, leading to risk uncertainties of factors of ten. The result, says Paul Portney, vice president at Resources for the Future, is that "almost everybody has the uneasy feeling that we're setting risks too high".

And then there is economics. Regulatory costs associated with risk management are estimated to cost between \$60,000 and \$175,000 million a year — as much as 15 per cent of total current federal spending and 3 per cent of the GNP by 2000. For decades, government agencies have been prohibited from considering such costs when making regulation, by the so-called Delaney clause of the congressional Food, Drug, and Cosmetics Act, which requires FDA to prohibit food that has any amount of a substance that causes cancer in animals, regardless of any other considerations. Although Congress itself passed an exemption to the clause in the case of saccharin, where rat tests probably gave misleading indications of human risk, the rule still holds for pesticide residues in food.

Now, however, federal and independent analysts are questioning the goal of blindly eliminating all possible carcinogens, regardless of the side-effects of regulation. They argue that the total effect of regulation — not just the effects of the substance under review — is the critical issue.

Leading the wave of big-picture evangelists is John Graham, director of Harvard

University's Center for Risk Analysis. Graham believes that the costs of regulation may actually be killing more people than the actual chemicals the regulations are intended to control.

Graham's argument goes like this: Poverty is an established risk factor for illness and premature death. In a 1980 study, men in families with annual income less than \$5,600 have a mortality rate of 140 per 10,000 population, compared to a rate of 80 for men who made between \$17,000 and \$22,000 a year. Or, as Graham puts it, "wealthier is healthier".

Government regulations cause some economic drain, both to industry, where they raise the cost of manufacturing and producing goods, and on the store shelf, where those costs show up in higher prices. More expensive goods mean a lower standard of living for everyone, but the effect can be most pronounced for those on the edge of poverty.

Graham calculates that every \$5 million in regulatory costs results in one life lost to the risk factors associated with poverty. Thus, for instance, if it costs \$10 million to eliminate a potential carcinogen that can be expected to cause only one death a year, the cost of the regulation in human lives would outweigh its benefits.

Not surprisingly, the theory has attracted its share of critics, although few doubt the central premise. "I'm not sure what the relationship is between EPA regulations and personal income, whether it's causal or coincidental", says Adam Finkel of Resource for the Future. But he, too, argues in favour of more economics in risk assessment. "We need to take a harder look at what we mean by the costs of something versus what we mean by its risks. Right now the balance is about 98 to 2 in favour of risks."

On Graham's side are such long-time risk assessment critics as University of California-Berkeley biochemist Bruce Ames, a long-time critic of government risk assessment. Ames points out that pesticides lower the costs of fruits and vegetables, making them more available to the poor. "I don't believe that chemical residues have ever caused cancer, yet it is well established that not eating fruits and vegetables can increase cancer risk", he says.

Inside the government, this argument has also found a receptive audience. "We're starting to look at the total combined burden to society, both health risks and economics", says EPA's Farland. By assuming that potential toxins should be eliminated at all costs, regardless of the larger picture, government regulators worry that they may have lost sight of their original purpose — overall health.

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Correction: Car-eating bacteria

The article on the biodegradation of motor cars in eastern Germany (*Nature* **350**, 453; 1991) unfortunately misspelled *Penicillium janthinellum* and misnamed the fungus a bacterium. □