What to Do about 'Unknown Risks'

Gio Gori raises very fundamental problems with risk analysis and, in particular, the way it has been used, or misused, by the U.S. Environmental Protection Agency ("Regulating Unknown Risks," Spring 2010). I urge scientists and risk analysts to consider his criticisms very carefully.

I find myself in agreement with much of the criticism of the EPA. But I disagree with the implied criticisms of those who estimate risks more carefully. Many of our disagreements are in the use of words and language.

Gori's title expresses the problem: "Regulating Unknown Risks." A risk is in itself a statement of probability that an untoward event will occur. In a real sense, it is always unknown. All we can do is to make an estimate of that probability, with uncertainty bounds.

Everyone considers risk every day. Even when we use historical data to estimate a risk, we use some sort of model. The simplest model is perhaps that next year's experience will be like last year's. But we can modify this model by making use of experience — maybe next year will be better than last year. The evidence for this must be considered, and there is inevitably uncertainty. The fact that we assume a model then invites the legitimate criticism that "all models are wrong." Yes — but some models are useful.

The problems come when we try to make decisions when little evidence exists. I agree with Gori that the EPA goes too far in assuming a far greater degree of reliability than is logically derivable from the data. In regulating trichloroethylene and other chlorinated hydrocarbons, the EPA assumed that animal data are predictive for humans and also extrapolated from a high dose to the much smaller doses in most situations, and tried to regulate at a risk level on 1:1 million in a lifetime, or about 1.70 million per year, pessimistically calculated. I have objected to this for over 30 years. The numerical value of the regulatory risk is far too low. I insist that regulators cannot do this consistently, and any attempt to do so is arbitrary and capricious and probably illegal on that ground alone. Unfortunately, I have found no one willing to challenge that procedure in court. If someone had, maybe we would have avoided two situations where scientific nonsense entered the courtroom and may have decided the outcome: the Woburn case and the Hinkley, CA case.

Perhaps more important in the long
run, the EPA in all reports implicitly assumes that the only uncertainty in its risk assessment is a statistical sampling uncertainty. The agency has consistently failed to state clearly that the biggest uncertainty is in the choice of model.

But what should society do when the estimation of the risk is very uncertain? Can one ignore it completely? Europeans argue for the “Precautionary Principle” without defining what the principle is. Loosely defined, it seems to be that if the risk is unknown, then the activity should be prohibited. This invites the question, unknown to whom? European Union regulators have proposed applying this to the use of depleted uranium. There is a large body of evidence that depleted uranium is not especially dangerous (except when a uranium-tipped shell hits a tank with you inside). This was well known to many people, but apparently not to the EU regulators. The U.S. EPA in 1990 suggested that the Precautionary Principle be applied to the effects of electromagnetic radiation at low exposure. That proponents of this proposal chose “EMF” to stand for “electromagnetic fields” seems to indicate their ignorance of the fact that, for 200 years, “EMF” has been used to describe Electro Motive Force. That they were also ignorant of other details and extensive studies that low exposure to electromagnetic fields has not been shown to cause adverse effects seems probable.

While I argue that the EPA set the level of risk for regulation far too low, I believe that Gori goes too far when he says that “cancer tests in rats do not predict cancer tests in mice better than tossing a coin.” The correlation between the results of such cancer tests is certainly not as good as the correlation of acute toxicity. But the carcinogetic potency of mice exposed to dioxin is perhaps 10 million times the carcinogetic potency of rats exposed to saccharin, whereas for the same chemical the potencies usually agree to within a factor of 10. The issue is how to incorporate this fact, with which few would disagree, into a model that is useful. But to use the model, one has to make the quantitative distinction between potent and nonpotent carcino gens. Since Bruce Ames and others showed that the number of chemicals that cause cancer in animals, albeit at high doses, exceeds earlier expectations, I suggested that it is no longer productive to make a distinction between a carcinogen and a noncarcinogen. Instead, we should concentrate on the value of the carcinogetic potency, including an upper limit of potency in appropriate cases. A noncarcinogen can then be defined as a material for which a statistically significant value has yet to be determined. At the time I proposed this, one prominent scientist said it was “the stupidest idea” he had ever heard. In the intervening years he relented, and so have many others.

Gori rightly comments on the principle usually attributed to Paracelsus that “the dose makes the poison.” I add the corollary, “More is worse, and less is better.” This is inherent in all the models used to discuss risk at low doses. I agree with Gori that the recent discussions of “endocrine disruptors” miss the mark. The proponents of active regulation for endocrine disruptors claim that the effects at low doses exceed the effects at high doses. This contradicts the Paracelsus principle. Hard though it is to justify that there are effects, although minute, at low doses by assuming a linear model to extrapolate from high doses, the difficulty for endocrine disruptors is far greater. The EPA would be wise to ignore them until it has improved its act on “ordinary” carcinogens.

Gori completely ignores the very strong theoretical justification for assuming a linear dose response relationship at low doses. If the pollutant in question produces cancers that are indistinguishable from cancers that occur naturally, then it is likely that, in one of the stages that led to cancer, the pollutant and the background are in the same way. Since the background (whatever it may be) has exceeded any threshold (or there would be no natural background of cancers), it can be shown graphically and analytically that a small amount of pollutant will introduce a small increase in the cancer rate. This argument is an old one. It is, for example, inherent in the mutistage theory as described by Peter Armitage and Richard Doll a half century ago. Harry Gues, Kenny Crump, and Richard Peto made this argument more general in their work in the 1970s. But the argument cannot be proven or disproven by more direct experiment or observation. I consider it a best estimate of the risk, with considerable uncertainty bounds.

Some scientists have tried to argue that low dose linearity would only apply to genotoxic compounds. If that is the case, then such materials as arsenic, asbestos, and benzene would be exempt. Yet these are the materials that the EPA most loves to hate! More important, there is nothing in the Guess, Crump, and Peto argument that would allow such a distinction. Indeed, the argument applies also to noncancer medical endpoints, such as lung problems caused by air pollution, for which the EPA officially assumes a threshold dose-response relationship. The EPA has so far refused to admit, or even discuss, this inconsistency, let alone correct it.

I know of no one who has refused to move from sea level to the mile-high city of Denver, with its higher natural background, because of the calculated risk from the increase in radiation exposure of about 1.200 in a lifetime. I have argued that the EPA and other regulators should take a risk of a little less than 1:10,000 in a lifetime as “acceptable,” since it is certainly accepted in this example. Many regulations would have to be relaxed, such as those noted above for chlorinated hydrocarbons, but perhaps arsenic would have to be more tightly regulated.

To relax a regulation when it is clearly excessive is crucially important for acceptance by the general scientific community. Almost all scientists accept that one has to be careful in exposing members of society to unnecessary risks. They would be willing to accept rigorous regulation of new substances if that regulation can be relaxed when better scientific evidence, either direct or indirect, becomes available. Since this has rarely, if ever, happened, there will always be a strong reluctance, such as that of Gori, to regulate.

I agree wholeheartedly with Gori’s complaint that regulators tend to screen out anyone who might bring an unwanted point of view to their science advisory committees. It is hard to prove, but I
have been informed that I have been screened out on more than one occasion for that reason. A related point: the EPA asks for public comments as part of its rulemaking procedure. Over the last 30 years I have sent in well over 30 public comments, many of which are available on my website (http://physics.harvard.edu/~wilson/). Only the most recent comment, sent this April, has ever been formally acknowledged. The other comments seem to have disappeared into a black hole. Ever since William (Bill) Ruckelshaus, I have personally brought this to the attention of EPA administrators, with no response. In contrast, NASA and the Nuclear Regulatory Commission publish public comments with a formal statement of their regulatory response.

Nor is the EPA the only group to be careless in its choice of persons to sit on its committees. In 1903, the British government asked Lord Kelvin, one of the brightest scientists of the 19th century, to be chairman of a committee to discuss arsenic hazard in the “Manchester beer epidemic.” In contrast, in 2001 there was a committee of the National Academy of Sciences/National Research Council to discuss arsenic standards. Dr. Allan Bromley, formerly a science adviser to President George H. W. Bush, pointed out to the president of the Academy that the committee chairman was not a member of the Academy, and that only one member of the committee, a member from Sweden, had ever seen anyone poisoned by arsenic.

The EPA and Gori have one thing in common: they have a long way to go in understanding, let alone proposing, a sensible way to regulate carcinogens.

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Response

Richard Wilson and I agree that we do science based on experimental and observational models. Those models cannot always be wrong, because airplanes fly and microwaves cook. Yet he may wish to consider that noncontroversial risks are indeed known, based on probabilities that depend on accurate data entries into models.

Leaving aside postmodern claptrap about science being opinion, model choice can affect uncertainty, but more so the absence of data entries derived from factual measurements with testable error rates. If such entries are unknown and unknowable, what could be the use of a model and related statistics, including sensitivity exercises à la Markow/Monte Carlo? Figsments of imagination in, and figments of imagination out. As noted in my article, even the Environmental Protection Agency agrees there is no way to know whether regulations protect health and safety.

Clearly, the EPA often regulates not only on little evidence, but also on no evidence or on fabricated evidence. Yet challenging the agency in court is nearly impossible and prohibitively expensive, with rare exceptions of no consequence. Reports from the National Toxicology Program still show that predicting carcinogenesis from rats to mice and vice versa is no better than tossing a coin. Hence, if we have to consider carcinogenic potency, for which animal model should it be, and under which default assumption models? Indeed, the strong theoretical justification for linear dose gradients, which Wilson fancies, is in itself based on whimsical assumptions of tumor initiation, promotion, and progression. In reality we still do not know definite modes of action for carcinogenesis, even as many hints suggest that each different cancer may have emerged from processes peculiar to its own.

Should we regulate nonetheless? Of course we should. But in the absence of reliable and testable data about risks, I sustain that precaution is rationally justified to the extent of minimizing exposures that still allow usefulness, and of keeping a robust and effective epidemiologic surveillance. My voice is and will be against regulations based on the odious imposition of fanciful and arbitrary default assumptions, falsely classified as science by a class of self-serving mandarins.

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