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IMPLICATIONS OF RISK ASSESSMENT PROCEDURES FOR HEALTH AND SAFETY POLICY

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Concerns over food safety have virtually exploded into public consciousness over the past two years, fueled largely by concerns over pesticide residues and other chemicals. The Alar scare revealed deep anxieties among the U.S. public over the safety of food in the U.S. and over the adequacy of regulatory mechanisms for ensuring that safety. Continuing debates over issues such as fungicide residues on produce, pesticide residues on imported foods, traces of dioxin in milk containers and the potential cancer-fighting value of foods like oat bran or cruciform vegetables suggest that these same types of concerns will grow in prominence in coming years.

In the past, food safety policy focused largely on risks from short term exposure to microbiological pathogens or chemicals that can cause acute illness and death. The goal of toxicological assessments in this context was to find the threshold dose, while the goal of regulation was to ensure that exposure always lay well below that threshold. In contrast, the new set of concerns that has emerged in recent years centers on risks from long term exposure to synthetic organic chemicals believed to contribute to chronic health problems such as cancers, birth defects and genetic damage. Current thinking regarding these problems assumes no threshold; any dose, no matter how small, is presumed to enhance the risk of contracting cancer or another similar health problem. Thus, regulators no longer face a problem of simply ensuring that the nation's food supply is safe; instead, they must determine how safe that food supply should be. Moreover, exposures to organic chemicals, and thus the risks associated with them, are typically low, while the costs of eliminating all traces are typically high, so that decisions regarding these chemicals tend to involve large tradeoffs. For this reason, regulatory action increasingly relies on quantitative risk-benefit procedures, which are mandated by law for most

cases involving pesticide residues on foods and food additives having noncarcinogenic effects.

A central problem in assessing these risks is dealing with the uncertainty that is an inescapable feature of chronic risk estimation. There are several reasons for this. One is that chronic health effects have multiple causes and are mediated by a multitude of factors, only some of which are observable; thus, science can account for part of observed variations in environmental outcomes. In addition, scientific knowledge is usually limited: Our understanding of the mechanisms of carcinogenesis, teratogenesis and mutagenesis is incomplete theoretically and empirically. For example, little is known about the long term effects of low exposures to synthetic organic chemicals like pesticides. Because of the low exposures and long time lags between exposure and the onset of symptoms, the linkages between exposure and effect are detectable in a reliable way only in cases of extremely toxic compounds. Yet the aim of policy is to prevent avoidable deaths. This preventive posture constrains policy makers to issue decisions in a timely manner as well, so that data collection is often not as thorough as might be desired.

These considerations imply that policy makers need to rely on estimates derived from indirect data and scientific inference. Over the past 15 years, a set of protocols has been developed for generating data from animal bioassays and combining environmental and biomedical models to obtain assessments of these potential risks. These protocols attempt to balance scientific rigor against regulatory needs for standardized procedures, limited data collection and timeliness. The estimates obtained from these protocols are heavily dependent on the assumptions made in modeling, adding an extra layer of uncertainty.

In sum, limited scientific knowledge and the need for timeliness create a situation where

the risk assessments used in quantitative policy analysis are characterized by substantial uncertainty owing to error in estimating risk and to variability in risk across populations that cannot be taken into account in risk estimates. Quantitative decision methodologies must address this uncertainty. The evidence suggests that the public is quite sensitive to the errors in risk assessment. The work of psychologists indicates that the public perceives as more hazardous effects that have greater uncertainty associated with them (for a summary see Slovic, Fischoff and Lichtenstein). The recent furor over pesticide residues on foods (e.g., Alar on apples) bears this notion out. The best data available suggest that roughly 85 percent of fresh produce in the marketplace have no detectable residues and that almost all of the remaining cases involve residue levels that are extremely small and well below what the U.S. Environmental Protection Agency considers the maximum safe levels. Yet much of the U.S. public believes that pesticide residues on foods pose a serious threat to public health. Policy makers also appear to be quite sensitive to these uncertainties, in part because of public demands for taking uncertainty into account in making regulatory decisions, in part (perhaps) because mistakes are the most visible indicator of poor performance.

The preventive posture of public health agencies suggests an asymmetry in preferences regarding uncertainty: Avoiding false negatives appears to be weighted much more heavily than avoiding false positives. This asymmetry is reflected in the posture of the public health profession and in much of the relevant legislation, which requires providing adequate safeguards for public health with a sufficient margin of safety. The latter condition can be interpreted as a safety rule formulation, where the risk estimate used is the upper limit of a one-tailed confidence interval with a significance level ("margin of safety") considered adequate

(Lichtenberg and Zilberman). In practice, regulatory agencies tend to construct "conservative" risk assessments where the upward adjustment to account for uncertainty is accomplished by using "conservative" parameter estimates and "conservative" functional forms.

Economists have tended to treat the output of these risk assessment procedures as fixed data to be used in cost-benefit or risk-benefit analyses. However, the procedures used in risk assessment bias policy choices. Some of these biases are intentional; for example, the use of "conservative" risk estimates enhances the attractiveness of more stringent regulation by inflating the benefits from regulation. Others, however, are unintended and, indeed, largely unrecognized. This paper discusses three major sources of unintended bias: (1) the practice of deriving "conservative" risk estimates by combining "conservative" parameter estimates; (2) the use of "conservative" specifications for dose-response functions; (3) exclusive reliance on point estimates of risk. In the following sections, I describe the type of bias introduced by each and its impact on food safety policy. The final suggestion suggests an alternative approach that would eliminate these sources of bias.

"Creeping Conservatism"

To account for the error arising in estimating risks quantitatively, regulatory risk assessors combine "conservative" estimates of each parameter entering a risk assessment model to obtain an overall estimate of risk. When "conservatism" is given formal statistical meaning, the estimate used will be the upper limit of a 95 or 99 percent confidence interval (see for example Anderson et al. for a description of EPA procedures). Suppose for example that the risk of cancer from ingesting residues of a pesticide residues on foods can be expressed as a

multiplicative combination of parameters describing the residue level, α, the ingestion rate, ϕ, the breakdown of the residue into toxic metabolites, β, and the toxicity of the pesticide and its metabolites, δ. (Given the narrow range of actual exposures, such a specification will provide a reasonable approximation regardless of the true functional relationships.) The standard regulatory procedure would involve estimating the upper limit of a (say) 95 percent confidence interval for each parameter and then multiplying these limits to obtain an overall risk estimate. Let $\alpha_{0.95}$ denote this estimate of α, $\phi_{0.95}$ denote the estimate of ϕ, and so on. The overall risk estimate ρ equals the product $\alpha_{0.95}\phi_{0.95}\beta_{0.95}\delta_{0.95}$.

This practice typically results in "creeping conservatism": The final risk estimate is associated with a confidence limit much greater than any of the individual parameter estimates. Consider the pesticide residue risk example given above. Suppose that the estimates used for every parameter are the upper limits of the 95 percent confidence interval. The probability that the true parameter exceeds the estimate is thus 5 percent. Assume also that these parameter estimators are independently distributed. The probability that $\alpha > \alpha_{0.95}$ and $\phi > \phi_{0.95}$ and $\beta > \beta_{0.95}$ and $\delta > \delta_{0.95}$ simultaneously is 0.05^4 or 0.00000625. Thus, the probability that the true risk ρ exceeds the "conservative" estimate is not 5 percent but 0.000625 percent; the confidence level associated with the risk estimate is not 95 percent but 99.9375 percent.

It is evident that the larger is the number of parameters used in the analysis, the greater the implicit confidence level will be. The usual rationale for more detailed modeling is to improve the accuracy of the estimate by incorporating as many contributory factors as possible. Yet the more detailed the risk assessment model is, the greater is the "creeping conservatism" effect. The confidence level associated with a two-parameter model will be 99.75 percent; that

associated with a four-parameter model will be 99.9375 percent; and that associated with an *n*-parameter model will be $(1-0.05^n)$ times 100 percent. The procedure of adjusting for uncertainty on a parameter by parameter basis undercuts attempts to construct more accurate models by imposing greater adjustments for uncertainty.

This procedure has a second negative effects. Different kinds of risks are more aptly modeled with different numbers of parameters. As a result, the confidence level effectively used varies from case to case. This makes it impossible to impose or even check for consistency in regulation across different risks.

Dynamic Effects

The choice of a functional form for estimating dose-response relationships has been one of the most hotly debated topics in the field of risk assessment. The problem arises primarily because of the low toxicity level of chemicals at typical food-borne exposures. To ensure detection of any existing toxicological effects at a reasonable cost, chronic toxicity is typically investigated at the highest biologically tolerated doses. Toxicity at the low exposures typically found on/in foods is then estimated by extrapolation from the high exposure dose-response data using a specific functional form. Obviously, the choice of functional form will influence the risk estimate to a considerable extent (see for example Munro and Krewski; Van Ryzin 1980). It turns out that it will also influence the type of policy chosen and the timing of implementation.

Classical toxicology posits an S-shaped relationship between dose and the risk of adverse health effects (Casarett and Doull). This is done partly for empirical reasons, since S-shaped curves like the lognormal best fit most data relating dose and the fraction of a population

exhibiting an adverse response. The theoretical rationale will be familiar to economists. Poisoning is assumed to be a quantal response determined by a threshold. Doses below the threshold result in no effects, doses above the threshold in observable effects. Individuals vary in terms of susceptibility, however; thus, the fraction of the population affected by exposure of a given level depends on the distribution of thresholds across the population.

The mechanism for cancer is assumed to be quite different. Carcinogenesis is believed to result from discrete, irreversible mutations that enable growth factors or disable growth inhibitors. Such a process gives rise to a dose-response relationship that can be expressed as an exponential function of a polynomial in the exposure level, the multistage model of carcinogenesis (Anderson et al.). For cumulative dose d, the incremental risk of contracting cancer can be expressed as $1\text{-}exp\{q_0 + q_1 d + q_3 d^2 + \ldots\}$. This function can have any shape. For low levels of exposure, though, as are typical of food additives or pesticide residues on foods, the linear term will dominate. For exposure levels near zero, which most food-borne exposures are, the incremental risk can be closely approximated as $1\text{-}q_1 d$. In regulating pesticides, the EPA uses the multistage model to derive an upper bound estimate of q_1 and then uses the linear approximation to estimate incremental risk (Anderson et al.).

While compelling at first glance, this procedure ignores a variety of factors implying that nonlinear specifications, particularly S-shaped curves, may be more plausible (see for example Portier). First, pharmaco-kinetic considerations imply that the relationship between the administered dose and the effective dose is likely to be nonlinear, which would make the dose-response relationship derived from animal bioassay data nonlinear (Cornfield; Hoel, Kaplan and Anderson; Van Ryzin 1985). Second, many carcinogens appear to be only weakly, if at all

mutagenic. The multistage model does not apply to these compounds, which include fungicides like captan and the EBDCs. For these compounds, promotion of pre-malignant cell growth appears to be the mechanism of carcinogenesis. Such a physiological process could result in nonlinear (S-shaped) dose-response curves (see for example Thorslund, Brown and Charnley). Third, differences in susceptibility or other background metabolic phenomena may generate S-shaped dose-response curves for a population, just as in the standard acute toxin case. Fourth, S-shaped curves may fit the available data better in some cases and would thus be preferred on strictly empirical grounds.

In sum, a variety of evidence suggests that the dose-response specification used by EPA is primarily a method for producing the most "conservative" estimates of risk that can be plausibly supported by the available animal bioassay data. Elsewhere, I have analyzed the effect of functional form on policy determination using a dynamic model of toxicity as a function of cumulative exposure. If toxicity is S-shaped, the use of a compound posing significant risk should be phased down over time, slowly while cumulative exposure is low and then more rapidly as cumulative exposure grows. If toxicity is linear, the use of the compound should be reduced immediately to the long term equilibrium level. If toxicity is concave, the use of the compound should be banned immediately. This analysis suggests that the procedure used by EPA biases policy analyses in favor of immediate bans on suspected weak carcinogens such as those found in foods and away from more gradual approaches such as phasing down usage until it reaches acceptable levels. The imposition of a more "conservative" functional form may thus increase the cost of food safety policies withouth appreciably increasing the marginal benefits from risk reduction, even after uncertainty has been taking into account.

Ignoring Uncertainty-Reducing Policies

Risk assessments typically produce point estimates of the final risk even though chemical contamination of foods and human exposures to chemicals on foods exhibit considerable variability and even though different policies alter this variability as well as affecting average contamination and exposure levels. Economists compound this error by basing policy analyses on point estimates alone, ignoring impacts of policies on variability of risk. Yet, as noted previously, this variability is important to the public and adjustments for it are written into much of the relevant legislation governing food safety.

As discussed above, the approach taken by the EPA and other regulatory agencies to adjusting for uncertainty is to make "conservative" estimates of potential damage under alternative policy scenarios. These estimates are then provided as a kind of certainty-equivalent data for cost-benefit or risk-benefit assessments. This procedure does more than bias policy toward more stringent standards, as is intended: It may also bias the type of policy chosen in favor of setting more stringent usage restrictions and against increased monitoring and enforcement. In other words, the use of point estimates alone biases policy toward strict usage regulation and away from variability reducing policies such as monitoring and research.

Consider the case of human health risks from pesticide residues on produce, where the outcomes of concern tend to be outliers, in the sense of occurring relatively seldom. Suppose that a pesticide leaves residues that result in a health risk ρ, expressed as the number of cases occurring in the population, a small fraction of the time α, so that the expected risk is $\alpha\rho$. Let the social cost of banning this pesticide be C_B. An alternative policy is an enhanced monitoring program that detects these residues an additional fraction of the time β at a cost C_M. If only

expected values matter, the pesticide should be banned as long as $C_B < C_M/(1-\beta)$. A "conservative" risk estimate of the type used by EPA treats the exceptionally high residue levels as normal occurrences and inflates the estimated risk to ρ. The cost per case avoided under a ban will be C_B/R, while the cost per case avoided under the monitoring program will remain $C_M/\alpha(1-\beta)\rho$, so that the ban will be preferred as long as $C_B < C_M/\alpha(1-\beta)$. Thus, whenever $C_M/(1-\beta) < C_B < C_M/\alpha(1-\beta)$, the use of a "conservative" risk estimate will erroneously indicate the superiority of the ban.

This case may well apply to the problem of pesticide residues on foods. The best data available suggest that roughly 85 percent of fresh produce in the marketplace have no detectable residues and that almost all of the remaining cases involve residue levels that are extremely small and well below what EPA tolerances, which are set conservatively. Clearly, these residues pose a significant risk only in a small number of instances. Increased monitoring could conceivably reduce the incidence of high residues to an acceptably low level at moderate cost, while usage restrictions are likely to impose much greater costs. Failure to consider enhanced monitoring as a potential policy response is thus likely to increase social cost without a corresponding increase in the marginal benefits of risk reduction.

Conclusion

Uncertainty has long been a central problem in assuring the safety of the food supply. The conditions determining the extent to which toxic organisms or compounds are present in foods are subject to considerable variability, as is human susceptibility to toxins. In the past, when the primary focus of food safety regulation was acute toxicity, this uncertainty was handled

by establishing thresholds containing large margins for error. More recently, food safety concerns have been shifting increasingly toward chronic toxicity problems such as carcinogenesis that have no thresholds. Faced with the problem of determining how safe is safe enough, regulatory agencies concerned with food safety typically build into risk assessments upward adjustments that serve to impose a sort of "uncertainty premium" (Lichtenberg and Zilberman) that increases estimated risk and therefore the benefits from risk reduction.

The goal of this approach is to bias risk-benefit or cost-benefit evaluations in favor of more stringent policies as a safeguard against the chance that the risks are higher than estimated. However, the ways in which this is implemented have some unintended and undesirable effects on policy formulation. Applying the upward adjustment to individual parameter estimates increases the bias introduced; the more detailed the risk assessment model is, the larger the upward adjustment. Moreover, this procedure makes it impossible to compare different policies for consistency. Choosing a "conservative" functional form for the risk assessment model, for example, EPA's practice of assuming a linear relationship between exposure and incremental risk, biases policy analyses toward immediate bans of chemicals and away from more gradual reductions in use that could be achieved at a lower social cost. The exclusive use of point estimates of risk biases policy analyses towards usage restrictions and away from uncertainty-reducing policies like enhanced monitoring.

These biases could be avoided through the use of probabilistic risk estimates, that is, risk assessment procedures that incorporate quantitative assessments of variability of risk and estimation error. Conservatism can be built into the final risk estimate, by specifying an upper confidence limit for the final estimate rather than for intermediate parameters or by choosing

"conservative" functional specifications. Risk assessment and economic policy analysis should be linked closely from the beginning, to ensure that the effects of alternative policies on variability of risk are incorporated into risk assessments. Changes such as these should improve the quality of information provided to policy makers and the general public.

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