TERATOGENIC - MUTAGENIC RISK OF WORKPLACE CONTAMINANTS: TRICHLOROETHYLENE, PERCHLOROETHYLENE, AND CARBON DISULFIDE

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QUANTITATIVE ANALYSIS AS A
BASIS FOR DECISIONS
UNDER TSCA

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Abstract

The language and the legislative history of TSCA leave ambiguous the extent to which formal analytical methods should be used to determine whether a chemical substance or mixture presents or may present an "unreasonable risk" of harm to human health or the environment. Decision makers implementing TSCA confront large uncertainties and great complexity in assessing the available information on chemical toxicity and exposure. Use of a probabilistic methodology such as decision analysis allows uncertainty to be included explicitly in the basis for decision. Case studies on specific chemicals indicate that quantitative approaches based on decision analysis offer significant potential for improvement of the regulatory decision process under TSCA. However, it is important that the analysis be perceived as a framework for discussion, debate, and investigation of sensitive assumptions rather than as a mechanistic formula for determining regulatory decisions.

Introduction

Passage of the Toxic Substance Control Act (TSCA) in 1976 was widely regarded at the time as a welcome improvement in environmental legislation. Unlike the language of the Clean Air Act or the Delaney Amendment, TSCA avoids calling for absolute elimination of health risks, requiring instead a balancing between the adverse effects on health and the environment and the benefits of a chemical substance or mixture. The impact of TSCA to date has been somewhat disappointing. Environmentalists note that few regulatory decisions have been made under TSCA, and they fear that the Reagan Administration's call for cost-benefit analysis under Executive Order 12291 may result in aggravating EPA's preexisting tendency toward "paralysis by analysis." Industry, on the other hand, is troubled by a lack of clear rules for determining what chemical uses are acceptable and what information should be gathered on chemical toxicity.

Difficulties with TSCA

While TSCA represents a step away from legislative requirements to eliminate risk and a step toward balancing the beneficial and adverse consequences of chemical use, the Act suffers from ambiguity compared to earlier legislation. What is "unreasonable risk," a term that is used repeatedly in virtually all the key sections of the Act but not defined clearly either in the Act itself or in its legislative history? Perhaps the closest approach to a clarification occurs in the following passage from the legislative history [1]:

> In general, a determination that a risk associated with a chemical substance or mixture is unreasonable involves balancing the probability that harm will occur and the magnitude and severity of that harm against the effect of proposed regulatory action on the availability to society of the benefits of the substance or mixture, taking into account the availability of substitutes for the substance or mixture which do not require regulation, and other adverse effects which such proposed action may have on society.

> The balancing process described above does not require a formal benefit-cost analysis under which a monetary value is assigned to the risks associated with a substance and to the cost to society of proposed regulatory action on the availability of such benefits. Because a monetary value often cannot be assigned to a benefit or cost, such an analysis would not be very useful.

The first part of the passage calls for a balancing of the probability of harm and the magnitude and severity of that harm against benefits that might be lost by placing regulations on the chemical substance or mixture in question. The ambiguity of the passage is that the balancing process needed for the determination of unreasonable risk is not described. Rather, the second part of the passage is phrased negatively: The balancing process does not require a formal cost-benefit analysis in which monetary value is assigned to the cost and to the risk.

Given this guidance, how is EPA to reach decisions, and how can industry understand EPA's decision process so it can anticipate these decisions in planning its business activities? Economists, analysts, and spokesmen for the current Administration might assert that despite the caveat in the legislative history that formal cost-benefit analysis is not required, some sort of cost-benefit balancing ought to be used in the decision process. But the application traditional of cost-benefit methods to assessing the consequences of chemical regulation does not account for uncertainty. While for a large number of chemical substances and mixtures there are grounds to suspect potential adverse effects on human health or ecological systems, it is rarely the case that the extent of these adverse effects can be estimated with any precision. It is also often difficult to forsee the economic consequences of a regulatory decision that will require a chemical to be removed from a major use or manufactured using an untried modification in the production process. Costs and benefits of regulation under TSCA will usually be uncertain. Yet the balancing process must be

carried out, explicitly or implicitly, to reach decisions, both within EPA and within individual chemical companies.

If analysis is to be useful in assisting this balancing process, it must deal with uncertainty. How this can be accomplished involves a simple concept: the use of probability as a way of communicating judgment about uncertainty. This concept is common sense to many people. We often communicate using this concept about sporting events (e.g., the probability that the Forty Niners will repeat their Superbowl victory next season), outcomes of elections (e.g., the probability that the Republicans will maintain control of the Senate next year), and weather (e.g., the probability of rain). In these situations the probability numbers serve as summaries of judgment about a multitude of complex factors. The judgments of political and sports experts and weather forecasters may be good or they may be poor. What probability provides is a way to describe uncertainties quantitatively so that we can discuss these uncertainties more precisely and incorporate them into our decision making.

Decision analysis provides a formal theory for choosing among alternatives whose consequences are uncertain. The key idea in decision analysis is the use of judgmental probability as a general way to quantify uncertainty. Decision analysis has been widely taught and practiced in the business community for several decades [2,3,4]. It provides a natural way to extend cost-benefit analysis to include uncertainty.

This paper will summarize briefly some work my colleagues and I at Decision Focus Incorporated have carried out for EPA to show how decision analysis might be used to assist decision making under TSCA [5]. I will first briefly review the concepts of quantitative risk analysis and cost-benefit analysis in order to show how decision analysis fits with these concepts and provides a natural way of extending them. Then I will illustrate the approach using a case study on a specific chemical, perchloroethylene.

An Overview of Quantitative Methods for Analysis and Evaluation of Chemical Risks.

The literature on analysis applied to assessment and evaluation of chemical risks is very extensive. There is wide agreement that quantitative analysis is useful as a framework for organizing information, for facilitating communication among the concerned parties, and for maintaining a separation between scientific information and the value judgments that are needed to provide a basis for decisions, but about which people may disagree. There is also wide agreement in the literature that quantitative analysis should not be expected to provide a mechanistic process or formula for selecting regulatory decisions. The responsibility for these decisions should remain with agency or company management. The difficult tasks of making the value tradeoffs between harm to health and economic impacts should come from top management, not from analysts or even worse, from assumptions buried in a computer program. Besides uncertainty and the difficulties of making tradeoffs between health and economic values, there are difficulties in dealing with distributional impacts: who will receive benefits under a given policy to control a potentially toxic chemical, and who will receive the costs? Quite often, the benefits and costs occur to different groups, and sometimes, they occur at different times. How benefits or costs occuring far into the future are to be treated is another area of difficulty.

There are relatively few case studies of quantitative risk analysis and cost-benefit analysis applied to chemicals posing a risk to human health and the environment. Those available include a variety of reports from committees of the National Academy of Sciences/National Research Council that have employed quantitative analysis methods or discussed the use of such methods in decision making by EPA or similar regulatory agencies [6,7,8,9,10,11]. While much of the analysis is commendable, there is little consistency in assumptions, methods, or even terminology. Within EPA's Office of Toxic Substances, it is difficult to identify and characterize quantitative analysis that might be used to facilitate the balancing process described in the TSCA legislative history.

There is broad agreement on what questions need to be addressed in carrying out quantitative analysis, but some disagreement on what to call the various steps of the process. The terminology I shall use below is somewhat arbitrary; my main purpose is to review the concepts.

Hazard Identification. Does a chemical substance or mixture cause adverse human health effects, such as cancer, birth defects, neurological damage, etc? Before beginning an analysis, it would be useful to have an unequivocal positive or negative answer, but that is rarely possible. The usual situation is that similarity to chemicals known to be toxic, toxicological testing in cellular systems or whole animals, and/or epidemiological studies provide evidence for suspecting that a given chemical agent may cause adverse health effects. The IRLG Guidelines [12] published under the Carter Administration recommend that "ordinarily," a single statistically significant positive result in one animal bioassay should be sufficient to conclude that a chemical agent should be considered for regulation as a potential human carcinogen.

Unit Risk Assessment/Assessment of Dose Response Relationship. Given that a chemical agent can induce cancer or some other adverse health effect in man, what is the incidence of the effect for a given level of exposure or dose? This question can rarely be answered very precisely, because for most chemical agents human data are not available, and even when such data are available it is usually very difficult to establish the doses of toxic chemicals to which people were exposed in an epidemiological study. The usual situation is that dose response relationships are estimated from animal bioassay data. EPA's Carcinogen Assessment Group (CAG) routinely produces such unit risk estimates for suspected carcinogens, using a standard set of statistical procedures and assumptions [13,14].

Exposure Assessment. What is the dose or the level of exposure of humans to the chemical agent? This question must be asked in the context of a given policy for controlling the uses and dissemination into the environment of a chemical agent. This control policy might be the present situation, a possible new regulatory policy, or a policy that a chemical manufacturer or distributor could choose to impose on his product. It is usually appropriate to assess the exposure of specific groups of people, which may depend on occupation, life style, purchases and uses of certain products, etc.

Risk Assessment. What is the incidence of the adverse health effects from the chemical agent? This crucial question for regulatory decision making might be answered by combining the unit risk assessment with the exposure assessment. As in the exposure assessment, the question must be addressed in the context of one or more specific control policies.

Risk Evaluation/Cost-Benefit Assessment. Given that risk assessment gives a means of estimating the change in the incidence of adverse health effects that will result from shifting to a new control policy, how are these health impacts to be balanced against the economic and other consequences that the policy change will have? This question involves making value judgments about health consequences, about economic consequences, and about the tradeoffs between them. These value judgments are very sensitive. There is great concern that using monetary values may be misleading, inappropriate, or unethical, yet there is little disagreement that the necessity of decisions requires tradeoffs between health and economic consequences to be made, either explicitly or implicitly, in the decision process.

Risk Analysis. The assessment of the incidence of adverse health effects in risk assessment plus the evaluation or balancing of health and other consequences of control policies in risk evaluation might be

termed risk analysis. Risk analysis is thus an assessment of what will happen under various control policies and an evaluation of these consequences according to some set of decision criteria. If the risks posed by a chemical agent are judged to be unacceptable under the current control policy, a set of possible new control policies is developed, and the best of these is selected, using the decision criteria either explicitly or implicitly.

Decision Analysis: Risk analysis can be expanded using judgmental probabilities to characterize uncertainties in the dose response relationship, the extent of human exposure, and the economic costs associated with control policies. What the expansion accomplishes is to provide a conceptual framework to separate the questions of information, what will happen as a consequence of control policy choice, from the value judgments that serve as decision criteria. We can then examine the extent of uncertainty and trace out its implications, rather than being forced into one set of assumptions to carry out an analysis. A frequent practice in risk analysis has been to use conservative, worst-case assumptions so that if the analysis errs, it errs on the side of protecting public health.

A Case Study Application: Perchloroethylene.

I now shall present a summary of an application of decision analysis to a specific chemical, perchloroethylene (PCE), a widely used dry cleaning solvent (also called tetrachloroethylene). The details of this application are presented in a forthcoming EPA report [5]. Perchloroethylene was selected for us by the staff of the EPA Office of Toxic Substances as representative of chemicals on which EPA needed to make an unreasonable risk determination under TSCA. Our analysis was carried out as an exercise in methodology development and not to support any specific regulatory activities by EPA concerning perchloroethylene.

Health Effects of Perchloroethylene. The basis for concern about perchloroethylene was primarily the result of an NCI bioassay, indicating that PCE induced hepatocellular carcinomas in B6C3F1 mice. A similar NCI bioassay on rats had given a negative result for PCE, as had a rat bioassay

carried out by Dow Chemical. The EPA CAG had prepared a risk assessment based on the bioassay data [15]. A meeting of the EPA Science Advisory Board Subcommittee on Airborne Carcinogens was called to review the CAG assessment as part of the determination of whether PCE should be regulated as an airborne carcinogen [16].

The CAG risk assessment included a unit risk estimate of the dose response relationship made following CAG's standard procedures [13]. A review of the SAB transcript showed that alternative assumptions were viewed as plausible by the members of the Airborne Carcinogens Subcommittee. CAG had fitted its usual multi-stage model to the data using a 95% upper confidence limit, a procedure which leads to a linear low dose extrapolation. Yet the SAB scientists noted evidence that PCE does not act directly on DNA, but indirectly through cellular toxicity. Given an epigenetic mechanism, a non-linear dose response relation might plausibly be expected. Similarly, while CAG has used the B6C3F1 mouse data as the basis for its extrapolation, scientists at the SAB meeting argued that the rat was more representative of the human metabolism. Finally, while CAG had extrapolated dose from animal to man using relative surface area, many scientific groups have recommended daily dose per unit of body weight as an appropriate scaling procedure.

Three instances were thus identified where there was uncertainty whether CAG's assumption was right, or whether there might be an alternative assumption that was more appropriate. The sets of assumptions are summarized in Table 1. If one assumes for simplicity that for each of the three issues either the CAG assumption or the alternative assumption is correct, then we have eight possible combinations or cases, only one of which represents the correct dose response relationship. Using the methods of decision analysis, we might assign judgmental probabilities to the eight cases. Such probabilities were used in our report, although the numbers are strictly illustrative. The probability numbers are less important than the concept of using a variety of cases based on alternative plausible assumptions. As we shall describe below, the magnitude of the change in

ISSUE	CAG ASSUMPTION	ALTERNATIVE ASSUMPTION
CHOICE OF SPECIES	B6C3F1 MOUSE MOST SENSITIVE SPECIES	RAT BETTER REPRESENTS HUMAN METABOLISM
SCALING OF DOSE FROM ANIMAL TO HUMAN	RATIO OF SURFACE AREA	RATIO OF BODY WEIGHT
LOW DOSE EXTRAPOLATION	MULTI-STAGE MODEL (EQUIVALENT TO LINEAR WITH USE OF UPPER CONFIDENCE LIMIT)	NONLINEAR RESPONSE BECAUSE OF EPIGENETIC MECHANISM (QUADRATIC RELATION USED AS REPRESENTATIVE)

EIGHT COMBINATIONS OF ASSUMPTIONS POSSIBLE

Table 1. Dose Response Assumptions for PCE Case Study

estimated cancer incidence from these changes in the dose response assumptions is nearly five orders of magnitude.

Exposure Assessment. Since perchloroethylene is used as a dry cleaning solvent and PCE vapor is easily monitored, estimates of PCE exposureare relatively straightforward to make from existing data in the literature. Table 2 summarizes the results. Based on NIOSH data [17], machine operators are exposed to an average of about 30 ppm of PCE vapor during the working day, equivalent to a continuous exposure of 45,000 $\mu g/m^3$. Other workers in commercial and industrial dry cleaners are exposed at a lower level, 10,000 $\mu g/m^3$, and workers in coin operated laundromat-dry cleaning facilities have an estimated exposure level of 6,000 $\mu g/m^3$. The number of workers exposed is based on projections from industry and census data.

Users of dry cleaning services are exposed when they visit the dry cleaning facilities and to a lesser extent from cleaned clothing. As shown in Table 2, the exposure levels are far lower than for workers. The highest level exposures are for customers using coin-operated laundry facilities in establishments that also have coin-operated dry cleaning machines. Urban residents are exposed to low ambient levels of PCE; the resulting exposure is less than for users of commercial dry cleaning services.

Control Policies for Reducing PCE Exposure. The amount of perchloroethylene vapor escaping from machines can be reduced by a variety of straightforward methods [18]. Better maintenance of machines, replacement of leaky gaskets and seals, and other "housekeeping" measures might, on the average, reduce PCE losses by 40% at little cost. In fact, these measures could result in an annual saving of the order of $10 million annually for the industry from reducing PCE purchases. A somewhat more costly option is the use of a carbon adsorption unit to recover PCE vapor from the air in the plant. Many plants already have these units, and if they were used throughout the industry, PCE losses and worker exposure would be reduced by an average of about 20%; exposure for service users and urban residents would be reduced somewhat less. Because of a credit for

CLASSES OF PEOPLE EXPOSED	NUMBER EXPOSED	ANNUAL AVERAGE EXPOSURE ($\mu g/m^3$)
WORKERS		
MACHINE OPERATORS	17,000	45,000
OTHER WORKERS	130,000	10,000
WORKERS IN COIN-OPERATED FACILITIES	33,000	6,000
SERVICE USERS		
COMMERCIAL CUSTOMERS	50 MILLION	5
COIN-OP CLEANERS	25 MILLION	10
COIN-OP LAUNDRY	37 MILLION	38
URBAN RESIDENTS	95 MILLION	0.2-4

Table 2. Exposure Estimates for PCE Vapor

PCE recovery, the net cost of these units for commercial dry cleaners is very low. Even when coin-operated units are included as well, the estimated net cost for using carbon adsorption units throughout the industry is only about $3 million annually. Putting coin-operated cleaners in a separate room from laundry facilities could reduce exposure for coin-op laundry service users by about 90%, at an annual cost of about $5 million. Finally, more expensive dry-to-dry machines could be used in commercial cleaners, reducing machine operator exposure by a third at a cost of $9 million annually.

Risk Assessment for Perchlorethylene. The above estimates for exposure, exposure reduction under controls, and human cancer incidence given exposure can be combined into a risk assessment. A summary of the results is given in Table 3. If the CAG assumptions for the dose response relation are used, the projected cancer incidence is about 350 cases per year, the majority of which occur in workers, with most of the remainder in service users. The lifetime probability of cancer for a machine operator is 23%, a high enough number that one would expect to see strong epidemiological evidence if these assumptions were correct. (Some epidemiological evidence does suggest an increased risk for cancer among dry cleaning workers [19,20], but not an effect of this magnitude.) If all of the control options discussed above were implemented, expected cases of cancer would be reduced about two thirds under the CAG assumptions, with a somewhat larger reduction in incidence among service users than workers. We might conclude, however, that even with these controls PCE would remain a significant public health problem.

If instead of the CAG assumptions we use the alternative assumptions on the right of Table 1, a very different picture emerges. The expected cancer incidence in that event is only one case per hundred years, a change of nearly five orders of magnitude. The lifetime probability of cancer estimate for a machine operator at 3×10^{-5} still is not negligible, because of the high level of the occupational exposure. The incidence and lifetime probability of cancer for service users and urban residents become

	CAG ASSUMPTIONS (PRESENT EXPOSURE)	CAG ASSUMPTIONS (FULL CONTROLS)	ALL ALTERNATIVE ASSUMPTIONS (PRESENT EXPOSURE)
EXPECTED NUMBER OF ANNUAL CANCERS:	347	112	0.01
WORKERS	181	84	0.01
SERVICE USERS	163	26	10^{-5}
URBAN RESIDENTS	3	1.5	10^{-8}
LIFETIME PROBABILITY OF CANCER:			
MACHINE OPERATOR	0.23	0.08	3×10^{-5}
COIN-OP LAUNDRY USER	2×10^{-4}	1×10^{-5}	10^{-11}
NEARBY URBAN RESIDENT	2×10^{-5}	1×10^{-5}	10^{-13}

Table 3. Summary of PCE Risk Assessment

negligible under the alternative assumptions.

Our report for EPA examines each of sixteen combinations of control options for each of the eight combinations of dose-response assumptions. The resulting 128 scenarios correspond to the end points of the decision tree shown in Figure 1. For each of these 128 scenarios we worked out the impacts on workers, users, and urban residents in the same manner as shown in Table 3.

Decision Analysis for Perchloroethylene. Decision analysis provides formal methods for selecting the best control decision in the face of uncertainty on the dose response relationship. Two sets of inputs are needed: (1) judgmental probabilities describing the likelihood of the assumptions and therefore of the eight dose response cases considered, and (2) a monetary equivalent value per case of cancer avoided so that health and economic impacts can be compared. While an important output of the analysis is the recommended control decision, this recommendation depends on the input judgments about the dose response uncertainty and the value of avoiding a case of cancer. Sensitivity analysis can demonstrate how changes in these judgments affect the recommendation on the control decision. The insights from sensitivity analysis are usually the most important results from decision analysis. These insights identify which judgments are critical in the selection of the best decision alternative, and which judgments are less significant because over a wide range of values the same decision alternative remains preferred.

We might illustrate by briefly summarizing the insights from our illustrative calculations on perchloroethylene. As base case assumptions we used value of one million dollars per case of cancer avoided, and probabilities of 20% to 50% for the CAG assumptions (implying 50% to 80% for the alternative assumptions listed on Table 1). For these probabilities the expected incidence of cancer is a few cases to a few tens of cases per year, and the most costly control alternatives are not judged worthwhile. (If the three CAG assumptions were to be judged certain or very nearly so, then the analysis would indicate that all of the controls

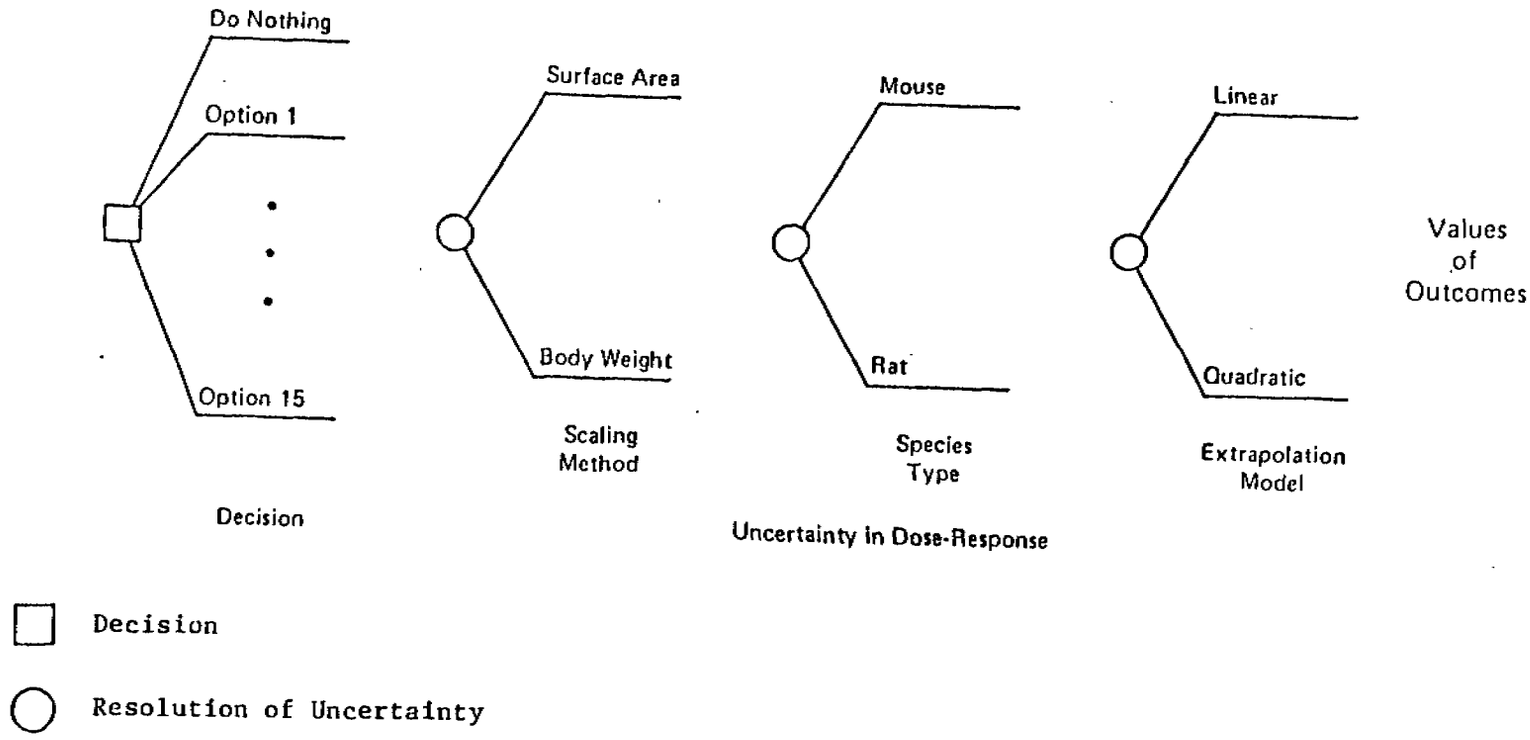

Figure 1. Decision Tree for PCE Control Analysis

would be worthwhile, since the reduction in cancer incidence times a million dollars then exceeds the annual cost for adding each of the control options.) Among the control alternatives, the option of better housekeeping and maintenance is clearly preferred to the present situation because reduced PCE consumption provides net economic gains and the health impacts to workers, users, and urban residents are all reduced. Carbon adsorption units are the next most attractive option, because their net cost is low and they afford significant reductions in exposure and therefore potential decreases in cancer incidence. Locating coin-op dry-cleaning machines in separate rooms may also be worthwhile if the probability of adverse dose-response cases and the value of avoiding a case of cancer are judged to be high enough.

Another important set of insights from decision analysis comes from evaluating what it would be worth to resolve uncertainty before making a decision. By such means as larger scale bioassays and pharmacokinetics research it might be possible to resolve which of the eight sets of dose response assumptions is a reasonable approximation to reality. How much should we be willing to pay to obtain such information? For the perchloroethylene case study, our illustrative calculations show the value of the information to be in the range of one to four million dollars per year.

Some Insights and Conclusions

Is the risk of cancer posed by perchloroethylene "unreasonable" under the language of TSCA? No clear answer emerges from the illustrative analysis. Whether a risk is unreasonable is not a matter to be determined from scientific evidence on toxicity and exposure, but rather a determination that will hinge on judgment. We concluded from our calculations that the uncertainty in annual projected annual cancer incidence from PCE was nearly five orders of magnitude, and such large uncertanties in health impacts may be typical for many chemical agents.

The major insight from the perchloroethylene case study comes from the comparison between risks to the workers, the users of dry cleaning services, and to the public that is exposed to low ambient levels of PCE in the air. If there is a significant incidence of cancer from PCE exposure, the effects will be predominantly among the workers rather than the users and the public. Calculations of the type we have carried out should be useful and illuminating not only to the regulatory agencies, but to individual company managements, workers, and consumers involved with a chemical agent. Many dry cleaning establishments are owned and operated by families, so that the management and the workers are the same people. Given that there is a suspicion based on animal bioassay evidence that PCE may induce cancer in man, some dry cleaning plant owners may wish to reduce PCE exposure by means such as carbon adsorption units whether or not they are required by regulatory agencies to do so.

Our assignment for EPA was to apply quantitative risk analysis methods to determination of risk for a particular chemical. The health risks for perchloroethylene turned out to be highly uncertain, but by using decision analysis concepts we were able to display this uncertainty in terms of alternative assumptions about the dose response relationship. Similar methods might be used to characterize uncertainties about human exposure to a chemical agent or about the costs to producers and consumers of a restriction on chemical use. (Evaluation of consumer benefits for a chemical substance in a market characterized by a high degree of competition and interproduct substitution can be a complex process. In our report for EPA [5] we have demonstrated how such a consumer surplus calculation may be carried out under a set of specific assumptions, which in a decision analysis might be viewed as uncertain).

Based on my research for EPA and other experiences as an analyst, I believe that uncertainty can be included into quantitative risk analysis on chemicals using decision analysis methods. The process of doing this for a specific chemical will typically require creativity and hard work from the analysts. It may not be possible to establish a single number for the

"probability of harm" as mentioned in the TSCA legislative history on the basis of hard scientific evidence; the "probability of harm" will usually be a reflection of scientific judgment, and the judgments of different scientists may often disagree. But probability is the right language for addressing the problem. An alternative to introducing probabilities is to make worst case assumptions. Such assumptions may be useful in determining upper bounds on the health risks of chemical agents so that low risk chemicals can be eliminated as subjects for regulatory attention. But when the worst case estimates are high, worst case assumptions on the extent of health effect incicence may serve little useful purpose for regulatory decision making and only frighten people who find they have been exposed to the chemical agent in question. What is needed is a careful examination and synthesis of the scientific information available so that regulators, chemical companies, and the public can balance the probability of harm against the benefits to be lost if the chemical agent is controlled or restricted.

Risk analysis, cost-benefit analysis, and decision analysis do not provide an easy means of calculating the right answers for regulatory decisions under TSCA. These decisions are highly complex and uncertainties abound. What quantitative analysis can provide is a decision framework where the complexities and uncertainties can be set forth and examined by those with an interest in the decisions and the time and motivation to explore the issues in detail. To the extent that decision frameworks based on quantitative methods can provide insights and improve the process of communication and consensus building, they will have a useful impact in improving industry and government decision making under TSCA.

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STUDIES ON PERCHLOROETHYLENE

Re. Carcinogenicity and Related Studies, Teratology, and Mutagenicity

Published/"Public" Knowledge

Study	Conducted By	Results/Observations
2-Year gavage study in rats and mice.	NCI	Increased incidence of liver tumors in mice but not rats.
2-Year inhalation study in rats exposed for 1 year and held for 1 year.	Dow	Tumor incidence of treated animals comparable to controls.
2-Year gavage study in rats.	Maltoni	Completion 1981; report 1982.
2-Year gavage study in rats (4 strains) and mice.	NCI	Completion (exposure) 1980; report 1981?
2-Year inhalation study in rats and mice.	NCI	Start 1981.
Rodent pharmacokinetics elimination	Schumann et al., 1980	Mouse metabolizes more than does the rat.
Human pharmacokinetics	Ogata et al., 1971 Monster et al., 1979	Man metabolizes very little; less than rat.
Biomolecular in mice.	Schumann et al., 1980	No binding with DNA.
Skin painting study in mice	van Duuren et al (1979)	Negative

Pure Tox

STUDIES ON PERCHLOROETHYLENE (cont.)

Re. Carcinogenicity and Related Studies, Teratology, and Mutagenicity

Published/"Public" Knowledge

Study	Conducted By	Results/Observations
Microbial mutagenicity	Greim et al., 1975 Henschler et al., 1977 NIOSH, 1977 Bartsch et al., 1979 EG&G Mason Research Inst., 1980	Negative.
	Cerna and Kypenova, 1977	Positive.
Cell transformation	Price et al., 1978	Positive (unvalidated test).
Cytogenetics	Dow Cerna and Kypenova, 1977	Negative
Mortality study of dry-cleaners.	NCI	Cancer incidence at several sites increased over U.S. population (smoking history or socioeconomic status not factored in).
	NIOSH	Ongoing.
Teratology	Dow	Negative.