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Approaches to Regulating Carcinogens

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PUBLIC PERCEPTION ABOUT CANCER AND THE LEGISLATIVE RESPONSE

The importance of cancer in U.S. policies about disease is illustrated by the attention focused on cancer research. The first institute of the U.S. Public Health Service to be devoted to a single disease was the National Cancer Institute (NCI), established in 1937. Initially a free-standing institute, it was incorporated into the National Institutes of Health (NIH) which was organized in the **1940's,** Thirty-four years after NCI's establishment, a nearly successful effort was mounted in Congress, in 1971, to separate NCI from NIH and to establish a National Cancer Authority, that would have set cancer further apart from other biomedical research activities. While the National Cancer Act of 1971 was unsuccessful in establishing a new authority, it elevated NCI to bureau status, a higher organizational level than all other institutes at NIH until the National Heart, Lung, and Blood Institute was also made a bureau. The 1971 legislation established **a** three-person cancer panel, appointed by and responsible to the President; no other disease has been singled out in such a way. The attention bestowed on cancer research reflects the importance of the disease to the public. It is the number two killer in the United States, the number one disease killer among people younger than 55, and it is the most dreaded disease (307).

In the 1960's and 1970's, public and congressional interest in cancer prevention was spurred by associations being drawn between environmental exposures and cancer. Congressional testimony mentioned associations between the environment and cancer, and several laws were enacted to provide Federal agencies with regulatory mechanisms to reduce exposures to carcinogens.

Public fear and dread of cancer is not likely to decrease, and despite the current antiregulatory mood, Americans still favor health and environmental regulations. A survey of 2,000 people, commissioned by Union Carbide in 1979, found continued public support of Government efforts "to protect individual health and safety and the environment." Seventy percent of those surveyed favored stronger measures to protect workers from cancer; **65** percent favored stronger measures to protect consumers from cancer (352).

Concern about cancer is likely to provide impetus for continued efforts to reduce its incidence and to improve its treatment. Efforts to improve treatment are seen as highly desirable and excite little controversy, but efforts to reduce cancer incidence by regulatory intervention generate great passion about whether the expected benefits from the regulations justify their costs. As is pointed out in the earlier chapters of this report, some uncertainty is associated with estimates made of the cancer risk posed by particular exposures. Part of the controversy about regulatory intervention, whether it is worth it or not, flows from those uncertainties, but controversy also stems from the fact that the regulations bring two societal goals into conflict. The majority of people want protection from carcinogenic risks, and at the same time want to reduce regulatory costs and burdens. Choosing between these two goals or reaching compromises between them will remain an important point of contention in policies about the control of cancer.

Several Federal agencies administer regulatory programs for the control of carcinogenic and other health risks to humans from chemical substances. These programs differ in their objectives and regulatory authority. Some were designed by Congress to deal with several different types of risks, including carcinogenic risks, in

the workplace or in consumer products. Others were designed to protect humans and the environment through control of toxic substances in air, water, and food.

Regulatory decisionmaking for control of cancer risks to humans is guided by specific legal mandates and administrative procedures and depends on technical determinations concerning the existence and magnitude of risk. This chapter first discusses statutory mandates related to carcinogen regulation, then moves to an examination of risk assessment issues. A concluding section focuses on the process of making regulatory decisions for controlling carcinogens.

STATUTORY MANDATES

Regulations of carcinogenic substances are designed to reduce health risks. The laws that require such regulations differ in whether they direct regulators to consider only health risks or to consider both health risks and other factors. The other factors to be considered may include the costs of reducing the exposure and the costs of foregone benefits from reduced availability of the substance.

Table 35 lists 10 laws under which some action has been or may be taken to reduce exposure to carcinogens. Of the applicable statutes, the Federal Food, Drug, and Cosmetic Act (FDCA), the Clean Water Act (CWA) of 1977, and the Toxic Substances Control Act (TSCA) specifically mention carcinogens. The remaining statutes provide for regulating all toxics, and carcinogens are included in the more general term. The list includes the laws most often discussed in relation to carcinogens but not all laws under which carcinogens might be regulated. For instance, laws governing transport of hazardous substances might be used to regulate carcinogens, and the U.S. Department of Agriculture regulates carcinogens in poultry and meat.

The earliest laws reflecting congressional concern about toxics centered on the food supply. Those laws, enacted around the turn of the century, established the Food and Drug Administration (FDA). In line with the importance society attaches to a safe food supply, the first law to apply directly to carcinogens was aimed at carcinogenic food additives. The Delaney clause, incorporated into the Food Additives Amendment of 1958, forbids the incorporation into food of any additive shown to induce cancer in humans or other animals.

The late 1960's and the 1970's saw the identification of carcinogens in various parts of the environment, and Congress provided legislative authority to regulatory agencies to reduce such exposures. The number and diversity of laws produces a "balkanized" Federal regulatory effort. Whether or not carcinogen regulation would be better accomplished under fewer, broader laws is a question worthy of consideration, but it is beyond the scope of the present assessment.

Bases for the Laws

Although many of the laws deal with other toxics in addition to carcinogens, the discussion here will focus on carcinogens to the exclusion of other health and environmental risks. The existence of the laws clearly states that Congress has seen cancer risks as deserving Government attention. At the same time, despite the fact that some of the laws are attacked as proposing an unobtainable risk-free society, Congress has recognized that cancer-risk management can sometimes involve balancing and comparing of risks against other societal goals. The 10 **laws** in table 35 can be divided into "risk-based laws" (or zero-risk laws) which allow no balancing of health risks against other factors, "balancing laws" which require balancing of risks against benefits of the substance, and "technology-based laws" which direct regulatory agencies to impose specified levels of control (306).

Risk-Based Laws

For this discussion, "risk-based" refers to legislation that provides for regulations to reduce risks to zero without considering other factors. The primary example is the Delaney clause which specifies that carcinogenic food additives are to be eliminated from the food supply. Section 112 of the Clean Air Act (CAA) and section 307(a)(4) of CWA call for the reduction of exposures to levels which allow an "ample margin of safety." Because Federal agencies do not accept threshold levels below which carcinogens pose no risk, strict interpretation of "ample margin of safety" would also require reductions to zero exposures. The Resource Conservation and Recovery Act (RCRA) is also risk-based, but no regulation about carcinogens has yet been issued under it.

When it enacted the Delaney clause, Congress was aware that over 1,000 substances were present as additives in the U.S. food supply. Many of those substances had been poorly tested (if at all) for acute toxicity and hardly any had been tested for chronic toxicity. ***Congress*** recognized that some of the additives might pose health problems, and the Delaney clause reflects its conclusion that no benefit could militate against banning a carcinogenic additive.

The most recent application of the Delaney clause was the proposed removal of saccharin from the "generally recognized as safe" (GRAS) list of food additives. This action, based on the finding that saccharin causes bladder cancer in rats, would then have resulted in the ban of saccharin from use as a food additive **(282).** Few people question that saccharin is a rat carcinogen, and the Delaney clause is clear: Saccharin should be removed from the market on the basis of the animal study. Peter Hutt, former General Counsel of FDA, points out that a zero-risk approach, such as the Delaney clause, may work reasonably well so long as there are substitutes. When no substitute is available, controversy flares, It flamed in the case of saccharin.

Because FDA had banned cyclamates on **the** basis of animal tests in 1969, the banning of saccharin would have meant that there would be no nonnutritive sweetener on the market. No one could have the pleasure of sweetness without the cost of calories. Citizens who objected to the ban, aided by postage-paid postcards inserted into cartons of saccharin-sweetened soft drinks, deluged Congress with mail. Congress delayed the imposition of the saccharin ban and called for more studies. In 1980, it continued the delay.

At the request of Congress, both OTA (282) and the National Research **Council (NRC)** (269) reviewed the scientific data and conclusions about saccharin and agreed with the FDA decision that saccharin is a carcinogen. The congressional decision to forestall action on **sac**charin can be viewed as the Congress reopening discussion about its earlier decision that benefits of carcinogenic food additives could not be weighed against their risks. It is aware of the evidence of risks (from animal studies) and benefits (from public outcry), and by delaying the ban, it is giving weight to the benefits.

Whether the saccharin moratorium presages an eventual voiding of the Delaney clause is an open question. Congress may retain the Delaney clause but, from time to time, exercise its prerogative to overrule agency decisions when it decides that benefits, whether measured or not, outweigh risks.

Comments are sometimes heard that the Delaney clause was appropriate for the state of knowledge in **1957** when it was enacted, but that times have changed. It is said that at that time there was general agreement that few substances were carcinogenic and that those few could be eliminated from commerce with little difficulty. However, more and more substances, including many useful and some apparently essential ones, have been identified as carcinogens. Some people make a connection between these discoveries and the apparent turning away from risk-based laws such as the Delaney clause.

Despite the fact that some of the laws written in the 1970's *were* technology-based or balancing (see below), section 112 of CAA, 1970, and RCRA, 1976, are risk-based. They direct that risks to health be reduced or eliminated without specifically calling for consideration of other factors, An important consideration in these

Table 35.—Public Laws Providing for the Regulation of Exposures to Carcinogens

Legislation (Agency)	Definition of toxics or hazards used for regulation of carcinogens	Degree of protection	Agents regulated as carcinogens (or proposed for regulation)	Basis of the legislation	Remarks
Federal Food, Drug and Cosmetic Act: (FDA)					
Food	Carcinogenicity for additive defired by Delaney Clause	No risk Permitted, ban of additive	21 food additives and colors	Risk	
	Contaminants	"necessary for the protection of public health. ." sec. 406 (346)	Three substances—aflatoxin, PCBs, nitrosamines	Balancing	
Drugs	Carcinogonicity is defined as a risk	Risks and benefits of drug are balanced.	Not determined	Balancing	
Cosmetics	"substance injurious under conditions of use prescribed. "	Action taken on the basis that cosmetic is adulterated.	Not determined	Risk. No health claims are allowed for "cosmetics." If claims are made, cosmetic becomes a "drug."	
Occupational Safety and Health Act (OSHA)	Not defined in Act (but OSHA Generic Cancer Policy defines carcinogens on basis of animal test results or epidemiology.)	"adequately assures to the extent feasible that no employee will suffer material impairment of health or functional capacity. ." sec. 6(b) (5)	20 substances	Technology (or balancing)	
Clean Air Act (EPA)					
Sec. 112 (stationary sources)	"an air pollutant. . which . . . may cause, or contribute to, an increase in mortality or are increase in serious irreversible, or incapacitating reversible, illness." sec 112(a) (1)	'(an ample margin of safety to protect the public health. ." sec. 112(b) (1) (B)	Asbestos, beryllium, mercury, vinyl chloride, benzene, radionuclides, and arsenic (an additional 24 substances are being considered)	Risk	Basis of the Airborne Carcino gen Policy
Sec. 202 (vehicles)	"air pollutant from any . . . new motor vehicles. . or engine, which. . . cause, or contribute to, air pollution which may reasonably be anticipated to endanger public health or welfare." sec. 202A(a) (1)	"standards which reflect the greatest degree of emission reduction achievable through. technology . . . available. ." sec. 202(b) (3)(a) (1)	Diesel particulate standard	Technology Sec. 202(b) (4) (B) includes a risk-risk test for deciding between pollutant that might result from control attempts.	Sec. 202(b) (4) (A) Specifies that no pollution control device, system, or element shall be allowed if it presents an unreasonable risk to health, welfare or safety.
Sec. 211 (fuel additives)	Same as above (2 l(c) (l)).	Same as above (2 1(c) (2) (a)).	—	Balancing. Technology-baaed with consideration of costs, but health-based in requirement that standards provide ample margin of safety.	A cost-benefit comparison of competing control technologies is required.
Clean Water Act (EPA) Sec. 307	Toxic pollutants listed in Committee Report 95-30 of House Committee on Public Works and Transportation. List from consent decree between EDF, NRDC, Citizens for Better Environment and EPA.	Defined by applying BAT economically achievable (sec. 307(a) (2)), but effluent levels are to "provide(s) an ample margin of safety." (sec. 307(a) (4))	49 substances listed as carcinogens by CAG.	Technology	
Federal Insecticide, Fungicide, and Rodenticide Act and the Federal Environmental Pesticide Control Act (EPA)	One which results in "unreasonable adverse effects on the environment or will involve unreasonable hazard to the survival of a species declared endangered . ."	Not specified.	14 rebuttable presumptions against registrations either initiated or completed; nine pesticides voluntarily withdrawn from market.	Sec. 2(bb) Balancing. "unreasonable adverse effects. ."	"Unreasonable adverse effects" means "unreaaonable risk to man or the environment taking into account the economic, social, and environmental costs and benefits. . ."

Table 35.—Public Laws Providing for the Regulation of Exposures to Carcinogens (Continued)

Legislation (Agency)	Definition of toxics or hazards used for regulation of carcinogens	Degree of protection	Agents regulated as carcinogens (or proposed for regulation)	Basis of the legislation	Remarks
Resource Conservation and Recovery Act (EPA)	**One** which "may cause, or significantly contribute to an Increase in mortality or an increase in serious irreversible, or Incapacitating reversible, illness; or, pose a. hazard to human health or the environ. ment. ." sec. 1004(5) (A) (B)	"that necessary to protect human health and the environment. ." sec. 3002-04	74 substances proposed for listing as hazardous wastes	Risk. The Administrator can order monitoring and set standards for sites.	
Safe Drinking Water Act (EPA)	"contaminant(s) which. . may have an adverse effect on the health of persons." sec. 1401(1) (B)	**"to the extent feasible. (taking costs into consideration). ." sec. 1412(a) (2)**	Trihalomethanes, chemicals formed by reactions between chlorine **used as disinfectant and organic chemicals. Two pesticides and 2 metals classified as carcinogens by CAG, but regulated because of other toxicities.**	**Balancing**	
Toxic Substances Control Act (EPA)					
Sec. 4 (to require testing)	**substances which "may present an unreasonable risk of injury to health or the environment. " sec. 4(a) (1) (A) (i)**	Not specified	**Six chemicals used to make plastics pliable.**	**Balancing: "unreasonable risk"**	
Sec. 6 (to regulate)	**substances which "present(s) or will present an unreasonable risk of injury to health or the environment," sec. 6(a)**	**"to protect adequately against such risk using the least burdensome requirement" sec. 6(a)**	**PCBs regulated as directed by the law.**	**Balancing. "unreasonable risk. "**	
Sec. 7 (to commence civil action against Imminent hazards)	**"imminently** hazardous chemical substance or mixture means a. substance or mixture which presents an imminent and unreasonable risk of serious or widespread injury to health or the environment. "	**Based on degree of protection in sec. 6**			
Federal Hazardous Substances Act (CPSC)	"any substance (other than a radioactive substance) which has the capacity to produce personal injury or illness "15 USC sec.	**"establish such reasonable variations or additional label requirements. necessary for the protection of public health and safety "15 USC sec.**		Risk	**"Highly toxic" defined as capacity to cause death, thus toxicity may *be* limited** to acute toxicity.
Consumer Product Safety Act (CPSC)	**"products which present unreasonable risks of injury. in commerce," and " 'risk of Injury' means a risk of death, personal injury or serious or frequent injury. " 15 USC sec. 2051** **"imminently hazardous consumer product' means consumer product which presents Imminent and unreasonable risk of death, serious illness or severe personal in jury." 15 USC sec. 2061**	**"standard shall be reasonably necessary to prevent or reduce an unreasonable risk of in jury." 15 USC sec. 2056**	**Five substances: asbestos, benzene, benzidine (and benzidine-based dyes and pigments), vinyl chloride, "tris"**	**Balancing: "unreasonable"**	**Standards are to be expressed, wherever feasible, as performance require. ments.**

SOURCE Office of Technology Assessment

two laws is that they deal with pollutants. Pollutants benefit no one, and their reduction or elimination improves the environment and public health.

A problem arises because eliminating the pollutants costs money. Furthermore, in the case of carcinogens, the evidence that a substance poses a risk is not always accepted by everyone. As a result, the cost of reducing exposure to a pollutant is often offered as an argument against the projected health benefits expected from regulation, and suggestions are made that the costs be considered against the benefits before regulation, even in cases where the law does not call for such considerations.

Balancing Laws

The "balancing laws, " such as the Consumer Product Safety Act (CPSA), the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), and TSCA, put a qualifying word, such as "unreasonable" in front of the word "risk. " This construction implies that some risks are to be tolerated, and, in practice, means risks from a substance are to be weighed against other factors in the process of deciding whether and how to regulate. TSCA requires that "the benefits . . . for various uses, . . . the economic consequences of the rule, . . . the effect on the national economy, small business, technological innovation, the environment, and public health" [TSCA sec. 6(c)(D)] be considered in deciding whether a substance does or does not pose an unreasonable risk.

Balancing is equated with some kind of comparison of benefits and costs, but none of the laws explicitly requires formal benefit-cost analysis. For instance, the Committee on Interstate and Foreign Commerce Report (65) on TSCA says that, "a formal benefit-cost analysis under which a monetary value is assigned to the risks" is not required. And a court decision about an action taken under CPSA declared that the Consumer Product Safety Commission "does not have to conduct an 'elaborate cost-benefit analysis' to conclude that 'unreasonable risk' exists" (145).

All of the laws provide for the regulation of carcinogens which threaten human health. In the case of the balancing laws Congress requires that other considerations be balanced against the health risk. In practice health risk signals an agency that it should consider regulation; the stringency of **that regulation is at least partially determined by balancing.**

Technology-Based Laws

CWA and CAA are, in general, technology based. For instance, CAA directs the Administrator of the Environmental Protection, Agency (EPA) to reduce particulate emissions to some percentage of existing levels. The regulations may be "technology-forcing" because new techniques may be required to achieve the reduction. In other cases, the laws specify that pollution control is to be achieved by using "best practical technology" (BPT) or "best available technology" (BAT). Such regulations do not force new technology, but bring all control efforts up to standards established by existing control technologies.

An important consideration of the technology-based laws is that EPA has not yet been required to produce studies to show that the imposition of new standards will improve public health. Imposition of the standards reduces exposures, and in the case of carcinogens, given a nonthreshold approach to carcinogenic risks, it follows that reducing exposures should improve public health.

The Occupational Safety and Health Act **(OSH** Act) requires:

> The Secretary, in promulgating standards . . . shall set the standard which most adequately assures, to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity . . . . In addition to the attainment of the highest degree of health and safety protection for the employee, other considerations shall be . . . the feasibility of the standards . . . (OSHA; sec. 6(b)(5))

In the sense that feasible has a technological meaning, the OSH Act can be considered as a

technology-based law. However, the Supreme Court may issue a decision in a case involving an OSH Act standard for exposure to cotton dust, that will determine whether or not benefits and costs have to be calculated to justify the standard. That case may not be heard since the Occupational Safety and Health Administration (OSHA) has withdrawn its proposed standard.

Freeman (131) has argued that the "technology-based" laws require balancing, pointing out that BPT implies balancing. How else can "practical" be defined? Likewise, deciding what is BAT involves balancing costs of the technology against the expected gains.

Doniger (95) cites a significant difference between technology-based and balancing laws. He suggests that once a hazard is identified under a technology-based law, the next step is to determine the best means to control it and then decide if there are any compelling reasons to back off from the best means. Under a balancing law, he says, once a hazard is identified, the next step is to quantify the risks it presents in order to balance those against costs of control.

The tripartite division of the laws—risk, balancing, technology—while useful, does not neatly describe all the laws when subjected to closer inspection. Complex laws contain sections that have different bases, and carcinogen regulations are generally developed under risk-based or balancing sections of the those laws.

An Example of Balancing

FDA can balance costs and benefits in regulating carcinogens in food except when the carcinogen is a food additive. An example of that balancing is the FDA (124) regulation of polychlorinated biphenyls (PCBs) in fish. FDA considered three possible levels for PCBs in fish from the Great Lakes (see table 36). Fish that contain PCBs up to the FDA-established tolerance level can be sold; those having more PCBs cannot be sold.

Few (perhaps no) people dispute that PCBs are a human health hazard. The acceptance of that fact is amply demonstrated by TSCA (sec. 6(e)) directing that PCBs be regulated. The information in table 36 may illustrate that once a risk is accepted as real, i.e., worthy of regulatory attention, the stringency of the regulation is set by economic or other factors. It is reasonable to assume that more cancer would result from PCBs at 5 ppm than at 1 ppm, but given the uncertainties of quantitative risk assessment, it is difficult or impossible to accept that the projected number of cases is accurate. Nevertheless, FDA decided that "the balance between public health protection and loss of food is properly struck by a 2-ppm tolerance. "

Table 36.—An example of Balancing Cancer Risk v. Revenue Loss. The FDA's Setting a Tolerance for PCBs in Fish

Proposed tolerance ppm	Projected cancer cases/vear	Estimated loss of revenue
5	46.8	$ 0.6 million
2	34.3	5.7 million
1	21.0	$16.0 million

The Precautionary Nature of the Definitions of Toxic Risks in the Laws

Reduction of exposures to carcinogens are intended to prevent cancer. Given the long latent period between exposure and overt disease symptoms, prevention must depend on the identification of carcinogens in test systems. The alternative, waiting for human evidence of carcinogenicity exposes some portion of the population to a carcinogen. Even if the substance is then withdrawn completely, the legacy of the exposure would be a continuing number of cases as some of the exposed people develop cancer. Reflecting these concerns, the definitions of toxic substances under which carcinogens are regulated do not require evidence of human disease. In accepting evidence from other sources, each of the laws is precautionary.

The Delaney clause is most direct; it accepts evidence of animal carcinogenicity as sufficient to ban a food additive. Section 112 of CAA calls for regulation of pollutants that "may cause . . . [an] increase in mortality;" RCRA **and the Safe** Drinking Water Act also use a "may" construc-

tion in defining toxics. TSCA directs EPA to require testing of new chemicals which "may present an unreasonable risk" (sec. 5), but has a more stringent, but still precautionary phrase, "presents or will present an unreasonable risk" in section 6 which authorizes regulating a toxic substance already present in commerce.

Regulatory Definitions of Carcinogens

The Delaney clause contains an operational definition for carcinogens:

> no additive shall be deemed safe if it is found, after tests which are appropriate for the evaluation of food additives, to induce cancer in man or animal.

Although the other laws do not define what properties of a substance make it a carcinogen, a number of Federal documents (e. g., 180,279) specify what technical results agencies will consider in deciding about carcinogenicity.

In most cases, animal data are the only basis for decisions about carcinogenicity. Seemingly endless arguments can be mounted about test results: that the tested animal may not be a surrogate for humans, that the dose was too high, that lesions in animals may not parallel human disease states. Given the current state of knowledge, those argument cannot be answered to everyone's satisfaction. In the absence of agreement among all concerned parties, agency statements about methods to be used in making decisions about carcinogenicity represent the Federal Government's position. It can only be expected that the methods will remain disputed until basic science provides more information about carcinogenic mechanisms and human response to carcinogens.

Degree of Protection

A balance between health and other considerations is struck by defining the degree of protection in each law. The Delaney clause, in which the balance is on the side of health, requires banning and the maximum degree of protection.

The other definitions of degree of protection in table 35 are not so clear, and at least one posed a difficult task for a regulatory agency. Section 112 of CAA is the basis for EPA's (111) proposed airborne carcinogen policy. It directs:

> The Administrator shall establish any such standard at the level which in his judgment provides an ample margin of safety to protect the public health from such hazardous pollutant [CAA sec. 112(b)(l)(B)].

The proposed airborne carcinogen policy (111) states that EPA has, "as a matter of prudent health policy, taken the position that in the absence of identifiable effect thresholds, carcinogens pose some risk of cancer at any exposure above zero. " The position that no threshold can be assumed for carcinogenicity makes it impossible to achieve an "ample margin of safety" unless zero emissions are imposed. However, EPA also decided that zero emissions for some substances would impose a too heavy economic burden, and that such controls were not what Congress had in mind. EPA solved this problem by proposing that BAT controls will be imposed, and if they leave an unreasonable residual risk, further controls will be considered (111):

> Final standards for source categories presenting significant risks to public health would, as a minimum, require such sources to use best available technology to reduce emissions. If, however, the risk remaining after the application of best available technology is determined to be unreasonable, further control is required.

A striking contrast in the use of the words "ample margin of safety" is seen in comparing CAA (sec. 112) and CWA (sec. 307). Under CWA, the first level of regulation is to be BAT which is also the language chosen for the proposed airborne carcinogen policy, after it had been concluded that an "ample margin of safety," the language of section 112, was unattainable. If after BAT has been applied, residual risk remains, "effluent standards" may be written to reduce effluents to achieve "an ample margin of safety" (see table 37).

Table 37.—Ample Margin of Safety as Used in Two Laws

	Clean Air Act	Clean Water Act
Level of protection	Sec. 112(b) (1) (B) *"ample margin of safety* to protect the public health. . ."	*Sec.* 307(a) (2) in accordance with sections 301(b) (2) (A) and 304(b) (2) sets "effluent limitations" according to BAT[a].
Regulatory language	No threshold level is assumed for carcinogens and an *ample margin of safety* is unattainable therefore BAT[a] is imposed.	
What happens if BAT[a] is judged inadequate?	Stricter measures can be employed to control residual unreasonable risk.	Sec. 307(a) (4) an "effluent standard" can be promulgated to provide "an *ample margin of safely."*

[a]*Best* available technology

AGENCY ADMINISTRATIVE PROCEDURES FOR CARCINOGEN REGULATION

The Administrative Procedures Act of 1946

The executive branch of Government administers hundreds of different laws. Agency procedures for carcinogen regulation as well as other subject areas are substantially dictated by the Administrative Procedures Act of 1946, specific formulas mandated by Congress within certain enabling statutes, and, in certain cases, by Executive orders. To varying degrees these formulas aim to safeguard individual rights and due process, while balancing potentially conflicting national goals and policies.

The Administrative Procedures Act (APA) was passed in 1946 after more than 10 years of painstaking study and drafting. Since then, there has been no major reform of regulatory procedures. According to Senator McCarran (228), who supported and explained the bill before the Senate, its purpose is to:

> . . . improve the administration of justice by prescribing fair administrative procedure . . . . [it] is a bill of rights for the hundreds of thousands of Americans whose affairs are controlled or regulated in some way or another by agencies of the Federal Government. It is designed to provide guaranties of due process in administrative procedures.

APA is generally applicable to all regulatory agencies and sets forth required procedures for agencies to follow when they engage in rulemaking (e. g., rules which set standards) and adjudication (e.g., licensing). The procedures involved may range from those which allow informal, mostly written, decisions without prior hearings, to those which require formal adjudicatory hearings complete with the right to cross-examination. While APA contains no specific guidance on informal decisionmaking requirements, different levels of procedural detail have developed depending on the kinds of issues involved. As has been noted:

> In terms of ordering the procedural values, one might organize (categories of administrative decisions) on a scale of maximum to minimum procedures. At the top of the scale, the hearing procedures employed may come close to the full adjudicative model, since the issues at stake resemble those decided in the civil or criminal process. Toward the bottom of the scale (e.g., planning and policy making) there may be few, if any, procedural requirements . . . . Even in these categories, however, certain procedural ingredients appear; in effect, notice and reasons requirements approximate a minimum procedural model (355).

Most of the agencies discussed in this study use "informal rulemaking" to make regulatory

decisions. Therefore, the minimal procedural requirements apply of providing public notice of proposed and final rules, and an opportunity for affected interests to comment. However, specific procedural requirements are imposed by some enabling statutes. TSCA, for instance, provides an opportunity for an informal hearing with cross-examination as a part of the rulemaking process. It goes beyond the more simplified APA informal rulemaking, but does not go as far as to require APA formal rulemaking procedures.

Judicial Review

APA and some enabling statutes provide for judicial review of the process by which agency decisions are made. In the case of informal rulemaking, the tendency is to require that agency performance not be, "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law" (5 U.S. C. sec. 706). Judicial review then examines the agency record to see whether the agency has provided notice, responded to comments, and given reasons for its actions to the public.

A more stringent judicial review is applied to formal rulemaking. In those cases, the court may "set aside agency action, findings, and conclusions found to be . . . unsupported by substantial evidence" (5 U.S. C. sec. 706). The court must decide whether or not the agency record contains substantial evidence to support the proposed action, but there is the presumption that the court will defer to agency expertise on technical matters contained in the record.

There is a tendency for judicial review of informal rules under the "arbitrary and capricious" standard to be increasingly stringent to the degree that it is converging on the "substantial evidence" standard prescribed by APA for judicial review of adjudicatory and formal rulemaking decisions (20). The reasonable conclusion is that both standards are coming to mean the same thing in terms of agency accountability when subjected to judicial review. As recently noted by Judge McGowan (231):

> If you're raising the question of the difference between arbitrary and capricious review and substantial evidence in the record, I think the judiciary is finally having to accept the fact that, because Congress has used them so loosely and so interchangeably, we have to assure ourselves that there is very little difference, if any, between them.

The practical effect of this merging of judicial review standards is to require closer judicial scrutiny of agency records and evidence in all reviewable actions. Some argue that agency flexibility and innovation, even to the extent allowed by APA, to meet the particular situation of each case has been almost eliminated by the threat of more critical judicial review. There is some concern that these developments have caused confusion in the courts and agencies, as well as worked considerable mischief on procedural regularity and the unifying function that APA was originally designed to perform for all branches of government and the public (355).

As the subject matter of regulation becomes increasingly complex, agencies are required to work more and more with incomplete or approximate data. Scientific uncertainty, compounded by the need to balance and value often conflicting goals, has raised questions about the continued workability of the present regulatory framework.

Regulatory Reform

The following remarks reflect some of the frustrations with the present system which are feeding the calls for reform. In a paper presented before the National Conference on Federal Regulation, September 1979, Richard Neustadt, then-Assistant Director of the White House Domestic Policy Staff, observed (275):

> [The **1946 Administrative** Procedures Act] predated most of the health and safety programs, concentrated on issues of procedural fairness, and took little account of the problems of economic impact and inconsistent policies.

Cutler (76), in expressing the views of the American Bar Association Commission on Law and Economy, has charged:

> [W]e have a regulatory system in which . . . the buck stops nowhere. We pursue each of our numerous and conflicting and competing goals with single-minded devotion regardless of the effect of one upon another.

Numerous regulatory reform proposals have been generated during the past few years, creating a widespread attack on the existing Federal regulatory system. The lack of effective balancing mechanisms in light of present economic and other national goals and policies has been raised with increasing frequency as a major failing. Furthermore, as observed by Costle (69), the concern for reform extends to cancer regulation:

> There is no question about the need for better management of the regulatory process. For example, I will be announcing in the next several days a national policy on the regulation of carcinogens ***[306].*** There are ***21*** statutes on the books that authorize the regulation of carcinogens. Thus, the necessity of having a consistent national policy is self-evident.
>
> But the issue of regulating carcinogens also illustrates a larger point, which is that we have not had a national road map of the cumulative effect of regulation, nor of where that regulation is taking us in terms of conflicting national goals . . . [We] have lacked a systematic way of tracking, effectively and intelligently, the multitude of regulatory activities that are ongoing every day.

Many of the recent regulatory reform proposals have called for substantive change through deregulation or severely restricted regulation.

Procedural Reforms

One category of reform proposals focuses on procedural improvements within the existing regulatory framework to make regulation more efficient, effective, and responsive to public needs. Through various means these efforts aim to improve agency administrative procedures, agency analytic and management capability, and public input for better regulatory decisionmaking. The executive branch, in the present and in previous administrations, has acted to improve the procedure through Executive orders. Legislative reforms are proposed in Congress.

Executive Order No. 12044 (Under President Carter) and No. 12291 (Under President Reagan)

In a major step toward regulatory reform at the executive level, President Carter issued Executive Order No. 12044 in March 1978. It directed each executive branch agency to publish a semiannual agenda of significant regulations under review or development, to provide greater opportunity for public participation, and to prepare regulatory analyses on all proposed regulations that may have major economic consequences (an annual economic effect of $100 million or more). To assist individual agencies in meeting the goals of this order, President Carter established the Regulatory Analysis Review Group, to prepare reports on particularly important proposed rules, and the Regulatory Council, to prepare a biannual regulatory calendar and deal with areas of overlapping and conflicting regulations.

This order had a significant and controversial impact on agencies charged by Congress with regulating risks to health, safety, and the environment. Office of Management and Budget (OMB) guidance encouraged the use of cost-benefit and other economic analyses to resolve health, safety, and environmental problems. However, there was no uniform policy or guidance for dealing with the methodological limitations of cost-benefit analysis—use of discount rates, how to value health and environmental benefits, how to allocate costs and benefits to different societal groups, etc. (20). In spite of the order's alleged faults and deficiencies, the Administrator and others at EPA, one of the agencies most experienced with this order, defended it as an encouraging beginning to resolving regulatory conflicts and shaping agency decisions in a manner that reflects overall policy objectives (69).

President Reagan issued Executive Order No. 12291 in February 1981. It preserved many features of the earlier order and provides for an in-

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creased role of OMB and cost-benefit analyses in deciding about regulations.

A conflict that arose under the old order is expected to continue, Some segments of society want to know the contents of a proposed draft regulation both when it leaves the agency and when it returns from OMB. Presently no public record is required of such drafts, and, in fact, such materials cannot be disclosed under the Freedom of Information Act. Protection of such documents is seen as necessary for the smooth functioning of the agencies and to allow regulators and decisionmakers to explore ideas and positions before going to the public with them. Resolution of the conflict between the public's right to information and the Government's desire for confidentiality may be reached in the courts.

Legislation

In 1979, the administration transmitted to Congress a bill that would have strengthened the reforms enacted by Executive Order No. **12044,** made them permanent, and applied them to all regulatory agencies, including the independent regulatory commissions (S. 755). It also would have overhauled key parts of the Administrative Procedures Act. Other bills of the 96th Congress proposed procedural changes, some of which paralleled portions of the administration's bill (e.g., S. **262, S. 755, S. 1291, S. 2147, and** H.R. 3263).

Several proposals require an agency regulatory impact analysis before issuance of major rules. Many require that the agencies set deadlines for rulemaking; and a schedule for review of significant existing rules. There are new provisions for agency rulemaking and adjudication, appointment of administrative law judges, and greater involvement of the Administrative Conference. Measures to increase public input include establishment of a Government-wide program of assistance to public interveners.

The Regulatory Flexibility Act of 1980 (Public Law 96-354) was enacted to lessen the impact of Federal regulation on small businesses and small Government units. This law requires, where there is a likelihood that agency rules may have a "significant economic impact on a substantial number of small entities, " that the agency prepare annual agendas for such rules and a flexibility analysis of each proposed rule. This analysis is for the purpose of explaining the rationale for agency action, considering flexible regulatory proposals, and examining alternatives which might minimize economic impact. While the scope of this law is somewhat limited, determined movement toward procedural reform is clear.

Structural Reforms Through Shifts in Oversight

Another category of reform proposals offers a more far-reaching approach by shifting existing regulatory authority to Congress, the courts, or the executive branch. The proposals call for structural reform in the sense that regulatory authority and, ultimately, political power are redistributed. They challenge the fundamental role of administrative agencies as they now exist, by imposing new outside oversight and review controls. Examples of these proposals include the legislative veto), the presidential veto, and the Bumpers amendment.

The Legislative Veto

A major study on Federal regulation by the Senate Committee on Governmental Affairs during the 95th Congress recommended that Congress substantially change its agency oversight processes to improve evaluation, coordination, and systematic review of agency programs. However, when it came to the legislative veto, it concluded that although this approach "may be appropriate in limited situations, the Congress should reject use of the legislative veto for regulatory agency rules . . . [and] should also refrain from routinely adding a legislative veto provision to regulatory agency statutes" (63).

Nevertheless, a number of reform proposals would enact various forms of the legislative veto. Depending on the bill, the approach would subject some or all agency proposed and existing rules to congressional scrutiny, with either House having authority to veto the rule

within a specified time (e. g., H.R. 1033, 96th Cong.; H.R. 460, H.R. 495, H.R. 532, H.R. 1858, and S. **1463,** 95th Cong.).

Serious questions have been raised about the efficiency of such an all-encompassing approach, particularly in complex areas of regulation, such as those dealing with carcinogens. The legislative veto option could conceivably result in technical decisionmaking being transferred from expert agencies to generalists in Congress. There may be some constitutional problems as well, concerning the separation of powers, congressional delegation of authority, the role of the President, and bicameralism where only a one-House veto is required.

Increased Presidential Authority: The Presidential Veto

Another structural reform proposal with far--reaching consequences would give the President increased authority over regulatory decisions. Again, there are a variety of forms to this proposal. One generating ongoing debate was developed by the American Bar Association (4). It would authorize the President to direct an agency to take up or reconsider and modify certain critical kinds of regulation, require cost-benefit regulatory analysis, and subject the President's actions to limited congressional review. While an agency would continue its normal rulemaking procedure, the President would have, in effect, final rulemaking authority over critical areas, since he could direct the agency to reconsider, modify, or reverse its decision.

As with the legislative veto proposals, a fundamental impetus for this kind of approach is the perceived loss of Government accountability resulting from overly broad delegations of authority to the agencies. Because of the many often conflicting national goals, to which the President must be responsive, and the narrower responsibility of single-mission agencies, greater Presidential authority is seen as needed for an effective balancing process and more responsible and accountable Government.

Questions similar to those raised with the legislative veto are again raised here. Constitutional and political issues related to overly broad delegation of legislative authority; Presidential efficacy, particularly when overseeing technical agencies; further delay and bureaucratic overload; and maintaining procedural safeguards are all concerns which must be examined with this approach to regulatory reform. Additionally, the shift in decisionmaking from the agencies, which have technical expertise, to individuals in the Office of the President who may lack technical expertise, can be viewed as inappropriate.

A Greater Role for the Courts: The Bumpers Amendment

Some structural reform proposals would shift power to the courts. A major example, which continues to spark interest is the Bumpers amendment, adopted by the Senate as a floor amendment in September 1979 (S. 111, 96th Cong., 1st sess., 1979). The amendment would do two things. First, it would remove the presumption of validity that accompanies a regulation when it is challenged in court. Second, it would require an agency to support the validity of a rule by preponderance of the evidence, a higher standard than either "arbitrary or capricious" or "substantial evidence. "

The amendment is seen as an attempt to curb problems associated with overregulation, and the courts would play a greater role and have greater influence. The role of the courts would extend to both overregulation and underregulation, since the courts also would be the forum for challenges that an agency is not regulating vigorously enough.

Levin (206) **says** that application of the amendment raises many ambiguities and difficulties of interpretation. While agencies could still be expected to conduct normal rulemaking activities, it appears that the proposal would require the courts to give little or no weight to an agency's decision. If so, the very reason for administrative agencies to retain expertise may be undercut. The likely outcome would be more litigation and challenge of regulations. Some observers have expressed doubts about the amendment's ability to facilitate more effective and ef-

ficient regulatory programs, especially in light of the increased workloads to come to the Federal courts. Others are of the opinion that agencies, knowing of the judicial review to come, would develop stronger cases.

Substantive Change: Deregulation

Some of the most drastic regulatory reform proposals call for deregulation or severely restricted regulation. These proposals raise a presumption against an agency's continued existence and legislative renewal except where there is explicit action to reauthorize.

One of the most popular concepts involved has been labeled "sunset'' -in other words, an agency or function will expire by a certain date unless there is enacted in the meantime a statute reauthorizing the activity in question. Various versions of regulatory sunset proposals have been put forth for a number of years (e.g., S. 2 and S. 445, 96th Cong.), Some would require that every regulatory program covered by a sunset requirement be reviewed at a minimum once every 10 years. The most drastic would call for termination of the program, with no provisions to safeguard against termination by inaction, if not authorized by Congress within this review period, Intermediate versions would require systematic review and reexamination of existing programs and legislation by the authorizing committees, with no automatic termination.

The most extreme regulatory reform is outright deregulation. In such areas as airline operations and natural gas production, this course has been taken. Apparently, the fundamental consideration underlying deregulation must be whether the objectives for which regulation was initiated can be accomplished by self-regulation in the marketplace. While most people view this approach as inappropriate for health, safety, and environmental matters, commentators have written about movement in this direction (59). For the present, the conclusions of the Senate study (63) of Federal regulation cited above provide insight into the question of marketplace possibilities for self-regulation:

> Generally speaking, "free market" solutions are not, in the environmental area, a viable option. The activities of a single polluter affect thousands and even millions of other firms and individuals, with whom there usually are no ongoing market relationships. Such relationships do not exist, in large part because neither firms nor individuals have clear property rights to environmental resources.

ESTIMATES OF RISK AND REDUCTION OF CARCINOGENIC EXPOSURES

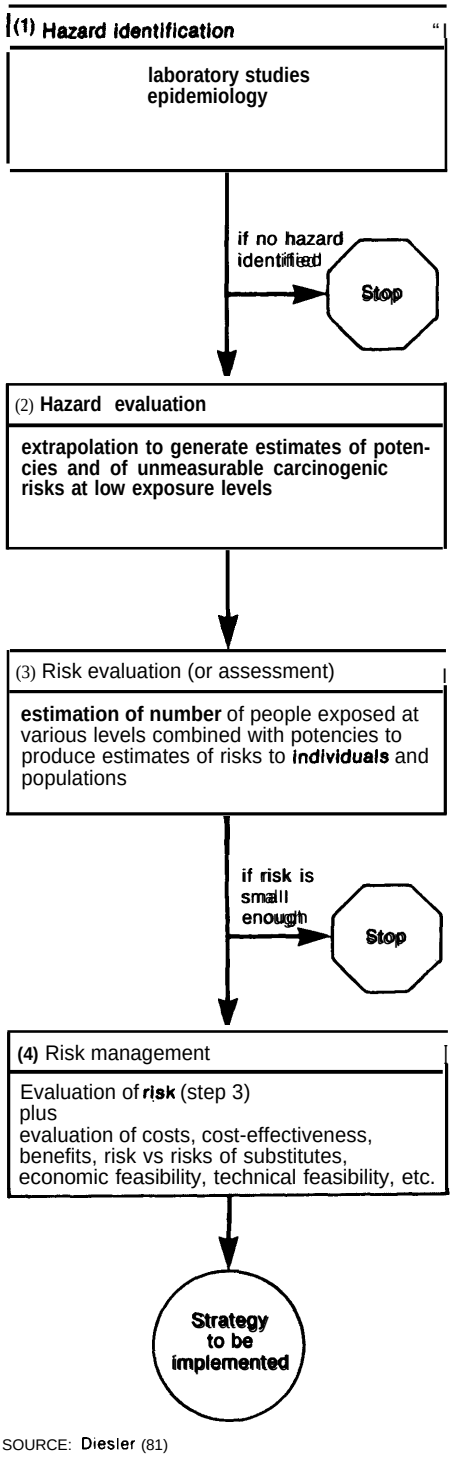
Risk Assessment

Recent years have seen a proliferation of organizations devoted to the study of risk. As examples, the National Academy of Sciences (NAS) recently formed the "Committee on Risk and Decision Making" that will consider how society and its institutions might better assess, compare, and manage health, safety and environmental risks. The National Science Foundation has an active "Risk Analysis Program" in its Division of Policy Research and Analysis, and several universities sponsor institutes for risk analysis.

A number of different terms—risk assessment, risk analysis, and risk evaluation—are used to describe the process of associating a specific risk with a substance. Figure 27 is an example of a three-step process for making an estimate of carcinogenic risk and a fourth step which lists other factors that may be considered in making a decision about reducing risk. The figure shows where the methods described in this assessment are used.

The first step, hazard identification, is necessary to separate carcinogens from other substances. Some laws, the Delaney clause as dis-

Figure 27.—Assessing Carcinogenic Risks and Considering Other Factors in Making a Decision about Risk Management



SOURCE: Diesler (81)

cussed above, require only this step to make a regulatory decision. The second step, risk evaluation, produces qualitative and quantitative expressions of the hazard associated with the substance. The quantitative expressions allow a rough ordering of hazards.

The third step, risk assessment, which can produce a quantitative estimate of the potential effect of the substance on humans, is limited by all the uncertainties involved in hazard identification and evaluation. Additionally, in this step, other uncertainties are introduced along with the estimates of the number of people exposed and the levels of their exposure. Some observers object to the third step because of these many uncertainties. However, uncertainties do not make it impossible to attempt to quantify risk assessments; they do affect the form the assessment takes and the form in which the result is presented.

The third step is necessary before quantitative comparisons can be made between risks and other factors. Such comparisons are shown in step **4.**

The critical function of step 3 is quantitative risk assessment. The generally good agreement that epidemiology and laboratory tests can identify carcinogens does not extend to agreement that currently available data and risk assessment techniques can accurately predict the level of human risk, and the usefulness of quantitative risk assessment is argued.

Some observers view quantitative risk assessment efforts, especially when applied to chronic health problems, including cancer, as premature. They see the techniques as uncertain, the results they produce as potentially misleading, and express concern that the users of the results do not appreciate the reservations attached to the numbers generated in quantitative risk assessments.

The advocates of quantitative risk assessment say that the methods are necessary to decide which of the many identified carcinogens present intolerable risks and which do not. To

counter the argument that the techniques are imperfect, they cite the great amount of interest in risk assessment and say that the methods are being improved.

Quantitative risk assessment is likely to take on increasing importance in Federal decision making about carcinogens. For instance, the requirement for benefit-cost analysis under Executive Order No. 12291 will result in greater demands for quantitative risk assessment. Additionally, the Supreme Court decision about workplace exposure to benzene (337) apparently requires that OSHA make some estimate of risk to support regulations. The fact that benzene is a carcinogen was not disputed in the case, but the court returned the proposed standard to the agency for reconsideration because OSHA had not found,

> . . . that the toxic substance [benzene at the level currently encountered in the workplace] . . . poses a significant health risk in the workplace and that a new lower standard is . . . "reasonably necessary or appropriate to provide safe or healthful employment''(20).

The requirement to show a "significant health risk" will surely result in greater pressure on OSHA to estimate the number of workers likely to suffer ill-effects from exposures. The pressures for use of risk assessment will probably increase, and opponents will continue to voice concern about its uncertainties.

Limits to Quantitative Risk Assessment

Rowe (316) draws attention to limits that he sees surrounding the accuracy of quantitative risk assessment. In particular he cites problems with choosing an extrapolation model, the widely variant estimates produced by the use of different models (see ch. 5), and the problems inherent in animal tests because of the relatively small numbers of animals that can be tested (see ch. 4). Rowe suggests that results of testing particular substances in short-term tests and bioassays be established as benchmarks. Then, as other substances are tested, they can be classified as less hazardous, equally hazardous, or **more hazardous than the benchmark substances.** At the same time, data about use and exposure can be obtained, so that the number of people at risk, along with potency, can be considered in deciding what next to do.

Importantly, in Rowe's scheme, a next step is to consider whether or not additional testing might change the conclusion reached on presently available data. To facilitate making that decision, Rowe developed a statistic to allow consideration of the probability that a test will provide information that might alter a previously made decision. Application of the statistic estimates the limits of knowledge that are attainable. Considering the limits of tests and extrapolation models will allow decisionmakers to select additional testing only when the tests will yield more definitive information. When that condition does not prevail, the decisionmaker can choose to do nothing or to consider various methods to restrict exposures.

"Trigger" Levels for Regulation

Individuals in their private lives accept nonzero risks. In some instances larger risks are accepted, presumably, because the benefits associated with the risk-taking are also large. In other situations, smaller risks are avoided, again presumably, because the benefits are seen as not worth even the small risk. Such observations lead to the suggestion that individuals balance risks and benefits in deciding which voluntarily assumed risks are "acceptable,"

Exposures to carcinogens in air, water, the workplace, and other environments are different from voluntary risks. In few cases is it possible for an individual to know the identity and magnitude of the risk. In many cases, the individual has no choice but to bear the unknown risk because contact cannot be avoided.

It is not necessary, in all cases, to quantify a risk in order to decide it is not acceptable. An example of such an unacceptable, unreasonable risk is the use of thalidomide by pregnant women. The association of that drug with children suffering multiple anatomic abnormalities led to a suspension of its use. A more recent example was the association of a particular brand of tampon with toxic shock syndrome. Before a quantitative evaluation of the lifetime risk of toxic shock syndrome was published, the manu-

facturer recalled the product. In these two cases, substitute products were readily available, and the cost of avoiding the risk was largely restricted to the lost sales of the manufacturers.

Regulatory agencies identify and quantify risks, and the ability to quantify risks has produced suggestions for managing risks based on their size. A small chance of risk can be set as a "floor," and substances presenting a risk less than the floor might be considered acceptable. Risks above the floor level would be divided into two groups. Intermediate risks would be considered for reduction, and benefits and risks would be balanced in making a regulatory decision. Above a still higher level of risk, no balancing would be necessary, and any substance presenting a risk of that magnitude or higher would have to be regulated (3).

Products of a quantitative risk assessment (see fig. 27, step 3) can be estimates of the lifetime risk of cancer to: 1) members of the general population; and 2) to members of highly exposed populations. These risks are expressed in scientific notation as 10^{-4}, 10^{-5}, 10^{-6} (or as fractions, 1 chance in 10,000, 1 in 100,000, and 1 in 1,000,000, respectively). Carcinogens differ a millionfold in potency as measured in laboratory animals, and more potent ones are associated with higher risks (10^{-3}) and less potent ones with lower risks (10-7).

Albert (3) and others have suggested that substances associated with individual lifetime risks of 10^{-5} might be considered as presenting risks so low that they require no action to reduce them further. Such low, negligible risks would represent a "floor" on risks. An idea of the magnitude of this risk is furnished by recalling that a 10^{-5} lifetime risk means that one person of 100,000 exposed at that level is expected to develop cancer from that exposure. Currently, about 20,000 of every 100,000 Americans die of cancer. Exposure of 100,000 people to a substance that increases risk by 10^{-5} could increase the number of cancer deaths to 20,001. Whether or not this number seems reasonable, it may be important to consider that a lifetime risk of 10^{-5} for the U.S. population (220 million people) is equal to 2,200 cancer cases in those people's lifespans. The annual number of cancer deaths from exposing the U.S. population to a 10^{-5} risk would be about 30, assuming a lifespan of 70 years.

A fundamental objection to the idea that some fraction of the population might be allowed to die because of exposure to a risk that is viewed as acceptable is expressed in an argument called "the murder of the statistical person." If the identity of the 30 people who died annually as a result of a 10^{-5} risk were known, there is little doubt that much greater effort would be expanded to reduce the risk. Objections to the idea of society deciding that some risks are negligible are raised by those who consider that statistical people as well as identified people deserve protection.

It is apparently more difficult to suggest a level of risk so high that it demands regulatory action than it is to suggest a level so low that it requires none. Nevertheless, toward the high end of the risk scale, agreement might be reached that an exposure that produced a lifetime risk of cancer of 10^{-2} (1 in 100) is so high that the Government should regulate it as a health risk with little or no regard for other considerations. The magnitude of this risk may be compared to the tenfold higher chance (10^{-1} lifetime risk) of cancer that is voluntarily borne by lifelong smokers (362).

Another consideration is that the low-level risks, those of 10^{-5} or less, add up. If there are ten 10^{-5} risks and the risks are additive, their total risk is 10^{-4}. (Of course, if synergism exists among any of the 10, the combined risk from both might greatly exceed 10-4). What is to be done about the next identified 10^{-5} risk? Should it be regulated, or should small risks, even if there are 100 or 1,000 or more of them go unregulated?

If agreement could be reached on such limits, risks above a certain level (10^{-3} to 10^{-2}) might be declared unreasonable no matter what, and risks below a certain level (10^{-5}) might be declared reasonable or acceptable or negligible. In between, the risks that range from 10^{-5} up to 10^{-3} or 10^{-2} would require balancing of the risks

and benefits to decide whether or not to regulate.

The inaccuracy of the risk estimates alarms many people. Crouch and Wilson **(72)** find "good correlations" between cancer rates measured in animals and those detected in humans due to exposure to the same chemicals. The number of chemicals for which data are available is small (fewer than 20) and the "good correlation" is good within a factor of 10 or 100. In other words, an estimated risk of 10^{-5} might be as high **as 10^{-3} or as low as 10^{-7}.**

Deisler (80) has approached the problem of the existence of many small risks by suggesting that a ceiling be placed on total risk in "exposure situations. " He cites industrial exposure as one situation and discusses a maximum allowable amount of cancer that might be set as tolerable for workplace exposures. As was pointed out earlier, estimates for occupational contributions to cancer vary from less than 5 percent to about **40** percent, and Deisler (80) suggests:

> . . . the first interim goal should be . . . to assure that industrially related cancer becomes less than a truly small fraction of today's total cancer incidence in the United States . . .

As an example of a possible interim goal, he suggests that workplace exposures be set so that they account for 1.5 percent of the total cancer burden. The 1.5 percent is only an example, and Deisler suggests that the selection of a goal might be negotiated in a public forum, possibly through a congressional commission.

When a ceiling is established, the risks within the exposure situation would be inventoried. If total risk exceeds the ceiling, the risk would be reduced by addressing one or more individual exposures. This appears to be a cost-effective system because the easiest-to-control, least costly-to-control exposures would be attacked first. If the inventory of risks totaled less than the ceiling, the ceiling could be reduced. The individual exposures in the inventory are expected to interact additively, but allowances could be made for synergisms if they occur. The ceiling also provides a method to deal with the identification of previously unrecognized carcinogens in an exposure situation. Such a carcinogen would be, as a first step, controlled to the point that the ceiling is not exceeded.

Despite the demonstrated existence of unacceptable, unreasonable (and generally unquantitated) risks, it has been impossible to assign "trigger" risk levels. Deciding on the "trigger," 10^{-3} or 10^{-2} on the high side, 10^{-5} or 10^{-6} on the low side would be difficult, and problems with the accuracy of the estimates and equity in that those who most directly bear risks may not most directly benefit are problems to be solved. Currently, quantitative risk assessment does not provide a tidy fix for the dilemma of deciding if and when to regulate. At the same time the fact that "acceptable" and "reasonable" risks are discussed implies that not all risks are equal and that society has the task to decide which are to be regulated and which are not.

LOCATIONS OF FEDERAL CARCINOGENIC RISK ASSESSMENT ACTIVITIES

Carcinogenic risk assessment involves a group of people considering the available evidence, drawing conclusions from the data, and, using methods they accept, deciding whether or not the substance is carcinogenic and, in some cases, estimating carcinogenic potency or human risk. Groups which have prepared statements about methods to be used in evaluating data differ in their interests and responsibilities, and their statements reflect the differences. In addition, there is much discussion about who should consider the data, apply the methods, and make the decisions.

Scientists in each regulatory agency now evaluate data about carcinogenicity of substances that may be regulated by their own agency. They may consider advice from expert commit-

tees in their decisions. The decision is then forwarded to the individual named in the appropriate law who announces the decision and his intentions to act on it.

The Office of Science and Technology Policy (OSTP) (281) proposed a change from agency-by-agency decisionmaking. It suggested that all carcinogenic risk determinations be made in a single governmental body. Representative Wampler proposed such a body in a bill he introduced; the American Industrial Health Council (AIHC) (10) and Markey (222) have also suggested central locations for making technical decisions for regulatory purposes. These proposals differ from each other, but all have in common a central panel of technical experts.

Panel proposals are all directed at decisions made by or for regulatory agencies. At the research agency level, the National Toxicology Program (NTP) has established a Peer-Review Panel of Experts to review draft reports from its bioassay program. The panel is to assure (273):

> . . . carcinogenesis bioassays have been carried out using the prevailing scientific state-of-the-knowledge and that the interpretations and conclusions reflect a logical and accurate analysis of the collected experimental data.

The panel can either approve draft reports or return them to NTP for revision. If panel members disagree about whether a report and its conclusions should be approved, a majority and minority report can be filed. The panel is composed of 14 experts from academe, environmental groups, and industry and began meeting in late 1980.

The issuance of the Interagency Regulatory Liaison Group (IRLG) guidelines (180) provides some uniformity to governmental decisions because all agencies are to use similar methods for evaluating risks. Agencies appreciate that consideration by nonagency scientists may improve their decisionmaking and may call upon experts to aid them. For instance, the proposed OSHA Generic Cancer Policy **(279)** allowed the Secretary of Labor to assemble a panel of Government experts to cooperate in making decisions about carcinogens. Such interagency workgroups are a common response of the Federal Government to complex and sensitive technical issues.

Some legislation" requires that agency decisions be discussed with advisory groups of non-Federal experts. Under FIFRA, EPA is required to refer any decisions to initiate a pesticide cancellation to EPA's Scientific Advisory Board (SAB). SAB review comes at a point in time after EPA has made a decision about whether or not the pesticide presents a toxic hazard, and it is an example of an advisory panel functioning in a review capacity.

FDA has made extensive use of technical advisory panels. In 1962, FDA was required for the first time to screen drugs for efficacy. Thousands of drugs were involved, and the task was immense. FDA asked that NAS assemble technical panels for different types of drugs and that the panels advise FDA about which drugs were not efficacious. The panels were quite successful and since then, FDA has added technical panels to advise about drugs, medical devices, and food additives.

The augmentation of agency expertise can be accomplished through calling on Government or non-Government scientists. There is now no legal requirement for such consultation in decisions about carcinogenicity, and advice can be rejected by the agency. Seeking or requiring advice from scientists outside the agencies is the least radical proposal for changing the current decisionmaking system. A number of other proposals would move some parts of decisionmaking about carcinogenicity out of the agencies altogether.

Three dimensions can be considered in setting up a decisionmaking apparatus. The first is personnel, whether the technical experts are to be from the Federal Government, the private sector, or both. Each of the proposals to be discussed below is specific about the organizational association of the experts. The *procedure* that might be used by the panel ranges from collegial to adversarial. The proposals tend toward the former pole; each provides the technical panel with a staff to develop information for the panel's consideration. The *power* of the panel can range from advisory to decisionmaking to

review. Most expert panels are now advisory, and the SAB is a reviewing panel. Some of the proposals call for the technical panel to make the decision for the agencies, others to review contested decisions.

OSTP Proposal for Decisionmaking

OSTP (281) divided Federal decisionmaking about carcinogens into two phases. Phase I is the identification and quantitative characterization of risks and encompasses steps 1 and 2 and part of 3 in figure 27. Phase II is making the regulatory decision to control the identified and characterized risk. OSTP proposes that phase I activities for all agencies be brought together and located within NTP.

The current responsibilities of NTP do not include phase I judgments for regulatory decisions. However, OSTP argues that just as NTP has a centralized coordination role in toxicological research so should it have a central role in interpretation of data.

Gilbert Omenn, an author of the OSTP paper (281), insists that decisionmaking about carcinogenicity should remain the responsibility of Federal officials. He makes the point that laws dealing with carcinogens are designed to protect public health and that Federal officials are entrusted with responsibility for administering the laws.

Having a panel of Federal officials decide about carcinogenicity is a major difference between the OSTP proposal and the proposals from AIHC and Representative Wampler. The latter two proposals centralize decisionmaking, but they would delegate carcinogen decisionmaking authority to new non-governmental organizations which would include non-Federal experts.

The American Industrial Health Council Science Panel Proposal

The AIHC (10) proposal for a science panel draws a distinction between scientific ("Phase I") and regulatory ("Phase II") decisionmaking as does the OSTP proposal. The science panel would be composed of "the best scientists available" and located centrally within Government or elsewhere. The panel would review existing data and not conduct or control research. Briefly, when a regulatory agency reached the point of considering regulatory action against a chemical, it would bring its data and conclusions about carcinogenicity to the panel. The panel would solicit additional data from industry, public interest groups, and other Government agencies and review all such data. It would assess the evidence and communicate its conclusions to the agency about whether or not the substance was a carcinogen. If sufficient exposure information and dose-response data were available, the panel would also evaluate the human hazard and risk posed by the carcinogen.

In the AIHC proposal, the panel would have to reach a decision within a certain time limit which would assure that it worked to a schedule. The panel would consider only scientific questions and its findings would not be binding. An agency could reject the panel's conclusions by explaining its reasons for rejection.

AIHC recommends that Congress establish a science panel consisting of 15 members who would assemble from time to time to consider data. It could appoint ad hoc members to workgroups to consider particular cases, and it would be provided with full-time professional staff to manage its workload.

Representative Wampler's National Science Council Proposal

Representative Wampler's bill to establish a National Science Council (NSC) was introduced on February 13, 1980 (H. R. **6521)** and reintroduced as H.R. 638 on January 5, 1981. It would establish a 15-member council to review decisions concerning chemical toxicity. A company or individual who objected to an agency's assessment of toxicity during the agency's adjudication could request NSC review of the agency decision. Subjects of meetings of NSC would be announced in the Federal Register and open to the public except when trade secrets or confidential information were discussed. The bill offers amendments to CPSA, FDCA, the

Federal Meat Inspection Act, the Poultry Products Inspection Act, the OSH Act, and TSCA. The amendments would make the decisions of NSC final with respect to scientific fact under those laws.

Mr. Wampler's proposal stipulates that NSC members would be appointed by the President to full-time Federal posts for 2 years and have appropriate staff support. This full-time service differs from AIHC's proposal. The AIHC Science Panel would convene "periodically to assess materials," but its members would maintain their usual employment while serving.

Judge Markey's Proposal for Legislative Branch Review of Risk Decisions

Each proposal so far discussed—convening of Federal committees, non-Federal advisory groups, or creation of scientific boards within or outside of the Government—seeks to improve decisionmaking before regulations are written. A strikingly different idea has been advanced by Judge Howard Markey of the U.S. Court of Customs and Patent Appeals.

Markey (222) proposes no change in the way agencies make decisions about carcinogenicity and regulations. However, he does propose that OTA, as an agency of Congress, review agency decisions about risks. The review would be initiated if a regulated industry or a public interest group objected in court to a regulation on the basis that the agency had made a mistake in science.

Markey goes on to **say** that if OTA or some other agency designated by Congress cannot reach an agreement about the correctness of the agency decision about risk, "OTA would turn to Congress, where the final decision on acceptable risk could be made by the people through their representatives."

Summary Comments About Technical Panels and Study of Their Feasibility

The number of proposals for risk determination panels almost guarantees that the panels will remain an issue in Federal policy about carcinogens. Establishment of such a panel would represent a significant change in the process used by the Federal Government to make decisions about health risks.

Proponents of panels claim they would improve the efficiency of the regulatory process. A panel would make technical decisions for all the agencies, which is seen as assuring consistent scientific findings. Secondly, a time limit imposed on panel deliberations would ensure that it complete its work quickly. Finally, a regulatory agency could initiate the panel review of data about a suspect substance, and therefore the review could take place when it best fits the agency schedule.

Public interest, labor, environmental organizations, and the Federal regulatory agencies oppose these suggestions. They see regulatory agencies as the appropriate and lawful locations for making decisions about risk. In general they see a science panel as another layer of bureaucracy that might hinder regulatory activities, and worry that a single panel might be more sensitive to pressure from interested parties. Furthermore, they see the division between "science" and "policy" in decisions about cancer as illusionary. They argue that such a panel might have the power to delay decisions by imposing a higher standard of proof that a substance was a carcinogen than is required by law. This would stymie preventive "precautionary" governmental action which they view as necessary to protect lives and health when certainty cannot be achieved.

Congress has appropriated $500,000 to FDA to place a contract to investigate the feasibility of a centralized science panel, and a report is expected in 1982. The results of that study should answer questions about how the panel might function and how, or if, scientific and technical decisions can be made separately from policy or regulatory decisions. The FDA-sponsored study may also reveal whether difficulties associated with chemical regulations have hinged on ***scien***tific or on regulatory controversies. If the study shows that scientific errors have seldom resulted from processes used by the Government or that the errors have been of little importance,

changes in the process of making scientific decisions would seem to have little merit. Conversely, if many examples of incorrect scientific decisions are found, changes might be appropriate.

MAKING REGULATORY DECISIONS

Possible Decisionmaking Frameworks

Each environmental health law seeks to reduce risks to the public health. Lave (204) discusses "frameworks" under which regulatory decisions can be made, and his categorizations are the basis for this section. He arrays the frameworks from that requiring the least information and analysis—the no-risk framework—to that requiring the most information and analysis—the benefit-cost framework. Some are familiar, describing the way in which decisions are made today; some suggest possible future directions.

1. The Delaney clause is most frequently mentioned as an example of the no-risk *framework.* It is a statement that Congress, concerned about the safety of food additives, has done the balancing of risks and benefits and has decided no benefits of food additives can outweigh a demonstrated cancer risk. FDA, the agency that administers Delaney, must show a risk before it bans an additive; it does not have to identify and measure benefits. Even if other organizations identify and measure benefits, FDA cannot balance benefits against risk.
2. The *risk-risk framework* requires a comparison of the risks associated with continued use of a substance to any risks generated by its use being controlled or discontinued. Generated risks would include those inherent in substitutes that might be employed in place of the substance. The best and most direct example of risk-risk analysis is the use of dangerous drugs to treat life threatening diseases. The risk from use of the drug can be compared with the risk of death if it is not used. A regulatory risk-risk determination is required under section 202 of CAA. As an example, a control device that reduced particulate emissions might, at the same time, produce chemical emissions. The risks from allowing continued particulate emissions would be compared to the risks from the chemical emissions.

   Direct risk-risk analysis could also have been applied to nitrites added to food if the Federal Government had sustained its case that nitrites were carcinogenic and deserving of regulation. Eliminating or reducing use of nitrites as a preservative would have increased the risk of botulism (severe food poisoning). Its continued use might be associated with a cancer risk. Under the risk-risk framework, a decision to ban, to reduce use, or to allow curent use patterns might have been made by comparing expected deaths from botulism and from cancer under the different levels of regulation.
3. *General balancing of risks against benefits* differs from the first two frameworks and parallels all others in that it allows consideration of effects other than health. Lave says that the framework is purposefully loose and vague; it requires enumeration of all effects, but weighing and balancing them, as well as deciding which to quantify, is left to the regulator. He includes determination of "feasibility" under the OSH Act and regulations of air and water pollution which require BPT and BAT under this framework. In reality there is no best available technology. It can always be made better, (e.g., by placing two control devices in series) but at some point costs are judged to be prohibitive. The hallmark of this framework is balancing of risks and benefits without quantification and analysis. Because of deficiencies in available and attainable information a general balancing approach is probably used in most decisionmaking.
4. Cost *effectiveness* compares the costs of different ways to reach the same goal. (The *Implications of Cost-Effectiveness Analysis on Medical Technology (285)* discusses this

method and its application to medical practice.) In general, the framework assumes a fixed budget and produces an allocation of resources (money) among different programs which share a common objective. Programs selected for funding are those that go farthest toward reaching the goal, in this case, reduced cancer incidence and mortality, at the least cost.

The expenditure of public funds is required to develop, promulgate, and enforce regulations. Private funds are expended to argue against regulations and to buy and maintain control devices. Cost-effectiveness techniques can be used to compare the total cost of a regulation, i.e., agency costs, industry costs, and costs passed onto consumers to the benefits of the regulation. Alternatively, cost-effectiveness analysis can compare benefits to either public or private costs separately.

Regulations that are expected to prevent the most cancers at the lowest cost would be identified in a cost-effectiveness framework. The difficulties of evaluating costs and benefits make it unlikely that the technique can distinguish between regulations of near equal benefits and costs, but distinctions should be possible between the most and least cost-effective.

Informal discussions with officials at EPA and OSHA suggest that Government costs are about the same for every regulation because each regulation is likely to be challenged in court, and each one requires about the same amount of staff time, whether its impact is large or small. Although this opinion was commonly expressed, no attempt was made to verify it. If it is true, an agency can select its goals by concentrating on those that will produce the biggest health benefit.

The regulatory budget strategy applies cost effectiveness to non-Government costs. Under it each agency might be granted an amount of private sector costs that its regulations could generate. Working within that amount, the agency would then propose regulations that it intends to promulgate and submit them for executive approval. This approach considers only costs to be borne by the private sector and could set an upper limit on those costs. OMB (280) reported that difficulties in estimating such costs make this approach infeasible.

5. *Benefit-cost or cost-benefit analysis* is similar to general balancing of risks against benefits but is more formal and quantitative. In this framework, all costs and benefits are expressed in dollars, and this analysis requires placing a monetary value on human life. After all items under consideration are converted to dollar terms, the benefits and costs are compared and if the benefits of the regulation exceed the costs, the decision is weighted toward making the regulation. Placing a dollar value on human life is one of the most controversial aspects of this method, and it is simply repugnant to many people.

   Lave claims the benefits of this framework are that it is the most flexible, requires the most information and analysis, and drives qualification where possible. Formal benefit-cost analysis is not now required by any carcinogen regulating law, but it is required by Executive Order No. 12291 where legislation does not forbid it, and it is frequently mentioned in plans for regulatory reform. A hearing of the Subcommittee on Oversight and Investigations (334) of the then House Committee on Interstate and Foreign Commerce provides a juxtaposition of opposing views of the applicability of the technique to regulatory decisionmaking.

Feasibility and Limits of Benefit-Cost Analysis

Traditional benefit-cost analysis is an economic tool that requires listing of all benefits and costs and assigning a dollar value to each. Carcinogen regulations involve the ultimate considerations—life and death—and opinions differ about whether or not a monetary value can be placed on life. In what ever way that controversy is settled, certain comments can be made about the usefulness of benefit-cost analysis.

In the case of a carcinogen regulation, expected benefits include the health gains from reducing exposure to the agent, and uncertainty is attached to the circulation of these gains. Presenting the expected health gain as a number does not add certainty to the estimate, but it adds to the estimate's importance. A frequent observation is that caveats and reservations attached to the numbers in the analysis are lost. The number of premature deaths to be averted ("lives saved") as well as the number of dollars to be spent to achieve the benefit take on lives of their own and are unencumbered by statistical reservations about accuracy. In this way, with no more information behind them, the numbers become more certain in the public's and the decisionmakers' minds. Too much reliance on imprecise numbers becomes a special problem in benefit-cost analysis which reduces the benefits and costs to dollar figures. This problem is commonly acknowledged but a practical solution is not readily apparent.

Many criticisms are directed at benefit-cost analysis. Lave **(204)** claims that a well-done analysis will always favor the status quo; change costs money. Change can be produced by going either from regulation to no regulation or from no regulation to regulation. Lave goes on to say that it would be surprising if the present state is truly the pinnacle of social evolution. If such a tilt toward the status quo exists when all measurements and calculations are accurately done, it is easy to imagine how a bias on the part of the analyst could affect the analysis. Not all economists agree with Lave's statement that benefit-cost analysis will always favor the status quo, and Freeman (132) cites the **NAS 1974 study,** *Air Quality and Automobile Emissions Control,* **as an** example of cost-benefit analysis which favored tighter controls.

Two other criticisms are directed at benefit-cost analysis. Equity considerations are not a part of benefit-cost analysis. For instance, the health benefits from a regulation accrue to those individuals whose risks are decreased; the cost of reducing the risks is borne by those who pay for the control devices or procedure. However, the situation before the control is implemented has the exposed people bearing a health risk which spares anyone in society from having to pay to reduce the exposure. The technique of cost-benefit analysis is silent about whether either case is just.

Another difficulty encountered with benefit-cost analysis is its inability to consider intergenerational effects. As a specific example, many substances are both carcinogens and mutagens. Such a substance may cause cancer in people exposed to it and mutations in their germ cells. The mutations are expressed in the next generation. Quantifying genetic damage is at least as difficult as expressing the value of a life in dollars.

A quite different problem in dealing with the future is economic. The discount rate chosen to project monetary costs and benefits is very important to these analyses, but there is no agreement about the appropriate rate, especially in inflationary times.

A response to objections about valuing lives in dollar terms is seen in the suggestion of the Conservation Foundation (78) that different types of analyses can be carried out under the benefit-cost rubric. It suggests use of the term "single-value analysis" to describe benefit-cost analyses which express all items in dollar terms and "two-value analysis" for analysis that compare "lives saved" to "dollars cost. "

The Conservation Foundation found "two-value" analysis appropriate for carcinogens when the major concern is death. It is less easily applied when additional considerations, such as damage to an ecosystem, are involved. "Multi-value analysis" is suggested as a method to consider three or more irreducible elements. It enables tradeoffs to be made, e.g., human health risk v. costs of reducing exposure, and ecosystem risk v. costs, but the analysis becomes more difficult. The claimed advantage of benefit-cost analysis (that it forces a detailing of what is being considered) is equally applicable to the one-, two-, and multi-value methods. The two- and multi-value methods involve balancing of health risk against other factors, and fit within Lave's third framework of general balancing of risks and benefits.

While two-value or multivalue benefit cost analysis may be attractive because of its rigor and its not placing a dollar value on life, it is not, strictly speaking, benefit-cost analysis. A benefit-cost analysis drives toward a single number, the quotient obtained when benefits are divided by costs. If the quotient exceeds 1.0, the benefits are greater than the costs, and the project should, on an economic basis, proceed. If it is less than 1.0 it should not. Two-value and multivalue benefit-cost analyses produce no such quotient. Instead they compare the benefits in one term (i. e., lives) v. costs (in dollars). The comparison is useful in a cost-effectiveness approach, where various approaches to a common goal can be ranked, but it does not produce a number that indicates "yes" or "no. "

A working panel of the NAS Committee on Principles of Decision Making for Regulating Chemicals in the Environment (263) concluded that:

> The systematic application of the tools of decision analysis and benefit-cost analysis can provide the decision maker with a useful framework and language for describing and discussing trade-offs, noncommensurability, and uncertainty. This framework should help to clarify the existence of alternatives, decision points, gaps in information, and value judgments concerning trade-offs.

Decision analysis, as described in the NAS report, is a careful detailing of regulatory options, expected outcomes and uncertainties of risks, benefits, and costs. Its "main contribution . . . is to organize information for the decisionmaker to assist him in his unavoidable balancing task. "

The NRC committee (263) endorsed the use of benefit-cost analysis and concluded that the technique is useful in making decisions, but that it should not be the only consideration in the decision. Furthermore it did not recommend continued research to improve the techniques because "highly formalized methods of benefit-cost analysis can seldom be used for making decisions about regulating chemicals in the environment. "

> If market prices and shadow prices are fully utilized to value economic efficiency effects, the initial list of noncommensurate effects of the decision will have been reduced to:
>
> - fully commensurate economic efficiency benefits and costs measured in dollars; and
> - noncommensurate effects, described and quantified in other units, of which the most significant are likely to be hazards to health and life, damages to the environment and ecosystems, and the distribution of benefits, costs, and hazards among individuals and groups.

The NRC definition of benefit-cost analysis does not require that all costs and benefits be expressed in a common unit (dollars), and it too would fit in Lave's third framework.

This assessment, which deals with the science and policy of making decisions about carcinogens, has emphasized uncertainties in determining risk. The Conservation Foundation (78) and NRC (263) also draw attention to uncertainties in projecting costs of regulations. Both sides of the benefit-cost analysis are difficult, subject to human error, and encumbered by uncertainties. Nevertheless, this method, whether one-, or two- or multi-value has its advocates, and it is increasingly mentioned as at least a tool to be used by decisionmakers.

An Alternative to Benefit-Cost Analysis for Making Regulatory Decisions

Sometimes the world seems divided between economists and lawyers. Economists favor decision frameworks that rely on quantitation and, in benefit-cost approaches, on converting all values into dollars. Lawyers are more comfortable with qualitative concepts as developed on a case-by-case basis under common law. In making decisions about risks under common law, courts rely on concepts of reasonableness of behavior, of duties and responsibilities to learn and to inform, of assumptions of risk that are made by different parties, and of contributory behavior. Application of these concepts is constrained by common law precedents, procedural rules, and rules about admissibility of competent evidence. Quantitative considerations of costs and benefits play a minor role (20).

Regulatory law differs from the common law. Its history is shorter, and it is constrained and governed by many specific and varied enabling statutes, the Administrative Procedures Act, the Regulatory Flexibility Act, and Executive Order 12291. However, more importantly, the regulatory agencies rely heavily on semiquantitative and quantitative risk assessment techniques, on experts, and, increasingly on a benefit-cost framework for decisionmaking. Agency emphasis on quantitation, which "invites . . . playing with the numbers" to reach certain analytical outcomes is producing a "lack of credibility or acceptance in the public and the regulated industries" according to Baram (20).

Offered against these criticisms of benefit-cost analysis are "the rational approach to decisionmaking that it allegedly fosters" and that "it emphasizes economic considerations, it retards excessively zealous regulations, it ensures that in general only incremental controls will be promulgated. "

> This has now become the central controversy for the regulatory agencies: How to implement their mandates to control carcinogenic risk in a fair, objective and accountable manner by using a "rational" framework (e.g., cost-benefit) which emphasizes economic cost factors, when the health and environmental benefits at stake are generally considered as being unmeasurable in economic terms **(20).**

Baram offers a decision framework that considers costs, but which also relies on qualitative considerations for regulatory agency consideration. His framework has six steps. The first two are common to any such decisionmaking scheme—hazard identification and risk measurement—but beyond those steps, he considers risk management options that he says are now overlooked.

1. *Hazard identification,* —This step involves the technologies discussed in this report and is initiated when a test shows a substance is a carcinogen. The development of the initial finding of hazard can be accomplished by Government or non-Government testing, because of a governmental rule requiring a test by private industry, or by presentation of a petition for rulemaking to an agency.
2. *Risk* measurement. --This step, too, involves some technologies discussed here. Baram emphasizes that agencies can improve their performance at this step.

   > Since agencies can use evidence in their rulemaking which would not be considered competent for admission in a trial in court, there are few legal protocols governing the quality of the evidence . . . [used] . . . in rulemaking. Clearly, there is a need for the agencies to establish such admissibility of evidence protocols and to bind themselves to the protocols if the competency and probative quality of the evidence used is to be improved and the confidence of the public and regulates in agency findings is to be increased. Costs will be a major factor in establishing such protocols . . . . Thus, it is imperative that agencies jointly address how to manage their resources for risk measurement collectively in the most efficient manner, and to establish collectively the costs to be imposed on industry for risk measurement when the measurement task is mandated for industry by law **(20).**

3. *Risk management options selection.* — This step is absent from current regulatory programs. It would identify and roughly assess the efficacy of regulatory and nonregulatory approaches to risk management. Regulatory options include both a) setting new standards and b) enforcing in-place standards. Nonregulatory approaches include a) recourse to common law, b) voluntary industrial standard setting, c) restrictions on future Federal procurement from sources of risk, and d) education or public disclosure programs.
4. *Economic and technical feasibility analyses.*—These analyses are required by some enabling statutes, Executive Order No. 12291, and the Regulatory Flexibility Act. They would focus on the management options identified in step 3.

   > The second, third, and fourth stages of measuring risk, assessing options, and costing options should ideally be kept separate and independent to ensure that risk measurement and option identification results are objectively arrived at on the basis of the best data and analytic methods for

risk estimation. This accords with the findings of many critics of the regulatory management of risk who have found a breakdown in risk measurement objectivity when it is influenced by cost considerations. This important reform need not be Congressionally mandated, but can be accomplished by the responsible exercise of agency discretion under existing statutes. It permits each agency then to conduct its fourth stage of economic and technical analysis in a structured fashion—as cost-effectiveness analyses of each option separately and in certain combinations **(20).**

5. *Ordering of risk management initiatives. —*

Having identified and measured risks and selected the most efficacious and cost-effective management options which are technically feasible, each agency separately (and in conjunction if several find the same carcinogen falling within their regulatory jurisdiction) should then . . . [order] . . . risks it will choose to manage on the basis of the carcinogenic risk reduction benefits to be achieved.

For instance, EPA might decide that the benefits of managing the carcinogenic risks of asbestos alone far outweigh the benefits of managing the risks of many chemical substances, and thereby would be in a position to allot rationally a proportionate amount of its resources to asbestos ***(20).***

6. ***Deployment of risk management options—regulatory and nonregulatory—for selected priority chemicals. —***

Finally, an agency is at the point where it can proceed to engage in rulemaking and other regulatory efforts, and foster the use of available alternatives to regulation, for reducing the risks from exposure to the selected priority chemicals. The use of alternatives in conjunction with regulation can be particularly appropriate in those cases where the number of exposed persons is relatively small (as determined in step 2); the alternatives are promising in terms of their efficacy for reducing the risk (as determined in step 3); regulatory approaches do not appear to be cost-effective or technically feasible (as determined in step 4); or the agency has determined that an optional allocation of its resources on the basis of its selected priority chemicals militates against promulgating and enforcing regulations (as determined in step 5). Thus, although the rational approach to risk management precludes regulating such chemicals, the agency assumes the continuing responsibility of fostering alternative approaches to manage such risks in keeping with societal values which support the protection of individuals from the dangerous acts of others. Following these actions, the agency has the responsibility to monitor results and take necessary corrective steps—e. g., in the case when the use of alternatives has failed, the agency may renew its efforts to foster the use of alternatives or decide to regulate (20).

Agencies can adopt either this specific risk management approach or some other approach, without congressional intervention or mandate. Baram proposes that agencies publish two rules to govern their use of the framework in order to guard against ad hoc or case-by-case subjective determinations. The first would describe the procedures it will follow; the second, any agency assumptions about subjective elements of its analyses.

This scheme shares drawbacks with any that involves ordering of regulatory goals. The decision that a risk is number one may be challenged, and concern about the accuracy with which the actual number one is identified may prolong the ordering process. Also, the publication of a number one risk, say, asbestos in step 5 above, might be accompanied with a list of "also-rans." Whether such risks would go unchecked because it is clear that agency resources would never reach them or whether voluntary risk reductions would flow from the publication is a ponderable question.

Baram's step 3 may be the most critical difference between what is now done and what might be done. Considering alternatives, discussing and comparing them, would better ensure the public and the regulated industry that the most efficacious approach was being selected. It also incorporates the cost-effectiveness framework to choose between alternatives. The scheme enjoys a powerful attractiveness in that it considers nonregulatory management of risks while reserving the regulatory "club" if it is necessary.

Making an Unreasonable Risk Decision

"Unreasonable risk, " the operational term in TSCA and CPSA, was of special interest to this assessment. It is a balancing term, and Congress decided not to define it, either in the laws or in the legislative history.

The House version of CPSA attempted a definition of "unreasonable risk" which involved comparing the severity and frequency of potential injury to the utility of the product, but the definition was deleted in the conference committee (145). In TSCA, the term was left undefined to allow maximum latitude to the EPA Administrator in making decisions. However, the House Interstate and Foreign Commerce Committee report accompanying TSCA states that unreasonable risk determinations involve **(65):**

> . . . balancing the probabilities 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.

OTA undertook two efforts to learn about the term "unreasonable risk" and how it might be applied in regulatory efforts. The first effort was a letter of inquiry to knowledgeable people and the second was a workshop held by the New York Academy of Sciences. They are described in appendix B.

Some responses to the letter viewed any risk of cancer as unreasonable in itself. Other respondents favored balancing the risk of cancer against benefits of the substance in question. These two groups 01 responses parallel two approaches to regulatory law that were discussed earlier. Another suggestion was that consumers should make their own unreasonable risk decision about consumer products. The Government would tell them of the risk; they would decide whether or not to accept the risk.

The same division between risk-based and balancing approaches to regulating carcinogens was reflected in discussions at the workshop. The workshop heard a number of talks and discussions favoring cost effectiveness as a method for deciding on regulatory approaches.

Unreasonable risk has been used as the basis of regulatory action in a limited number of cases. To date, EPA has promulgated three regulations under TSCA to limit unreasonable risks from substances in the environment. TSCA required that EPA regulate PCBs; EPA regulated fully halogenated chlorofluoroalkanes, which threaten the ozone layer in the atmosphere, and it prohibited a company from disposing of 2,3,7,8-tetrachlorodibenzo-para-dioxin ("dioxin") at a particular facility. The few regulatory actions so far undertaken do not provide a coherent picture of how EPA will make unreasonable risk decisions. It is noteworthy that each of these actions dealt with a substance associated with cancer.

In response to a General Accounting Office (141) report, EPA stated that it had not developed "decision criteria" to make unreasonable risk decisions in the course of premanufacture review under section 5 of TSCA. The agency has considered drawing up such criteria, but found that the amount and variety of information to be weighed in such decisions precluded their developing criteria. Premanufacturing notices (PMNs) (see ch. 4) are considered on a case-by-case basis, and EPA considers that approach satisfactory at this time.

EPA assembles health and economic data about a substance considered for regulation and, in different offices, carries out a risk assessment and an economic assessment. These two assessments are then used to reach a decision about unreasonable risk. EPA guidelines (101) for making judgments about carcinogenicity, govern risk assessments. EPA has not yet published information about how it will carry out economic assessments (20). Each assessment carries with it some uncertainties and the quality of the data that go into the assessments varies, but eventually the results of the assessments go to the Administrator (78):

> The last stages of determining unreasonable risk (under TSCA) involve the Administrator of EPA, the Assistant Administrator for Toxic Substances, and perhaps one or two other high-level

officials evaluating the evidence and analysis, sorting through their own personal values, perhaps testing the political winds, and then coming to a conclusion. It is definitely not a process that can be subjected to tidy rules or guidelines.

The Administrator, who is appointed by the President, makes and publishes the decision. He is responsible for the decision made, and if it is shown to be incorrect, he can be removed from his position.

Not "Unreasonable Risks" and What To Do About Them

It seems likely that testing of chemicals will reveal a substantial number that present "limited" but not "sufficient" evidence for carcinogenicity. The words "limited" and "sufficient" are borrowed from the International Agency for Research on Cancer's (IARC) classification (see ch. 4 and app. A). In the case of "limited," the available evidence supports the idea that the substance is a carcinogen, but it is less than "sufficient" to force a conclusion.

A regulator might consider a substance for which only "limited" evidence exists as deserving of regulation. He might come to this decision because many people or very sensitive people, such as young children, were exposed or because a substitute was readily available.

Whatever his reasons for considering regulation, economic assessment of most chemicals in commerce will probably show that significant costs would attend any regulatory scheme. In other words, often there may be a small risk and large costs. With those assessment results, it is likely that further analysis will not result in an answer that says "regulate" under the formal, rigorous balancing mechanisms discussed here.

A regulator who sees his first responsibility to be the protection of public health might be uncomfortable with that decision, and the producer of the substance, although not wanting to be regulated, might be uncomfortable also with continuing exposure at current levels. Methods to deal with these situations through discussion and incentives might reduce the antagonism between regulators and the private sector and promote public health (19, 20).

RESPONSIBILITY FOR MAKING DECISIONS

Quantification of risks and benefits is never likely to be so precise that estimates of these variables can be plugged into a formula to produce a number that dictates a decision. Instead, after all the analyses, a decision about whether a risk is acceptable or unacceptable and reasonable or unreasonable will be made by a few individuals. Those judgments reflect societal values and would, ideally, be made by citizens as a whole. In our form of Government, elected representatives are responsible for expressing societal values, and this responsibility is sometimes delegated by elected representatives to executive or judicial branch officials.

Executive Branch Decisions

The size and complexities of Government have resulted in elected representatives delegating authority to make judgments about acceptable risk to executive branch agencies. A number of commentors, including Markey (222), point out that many executive branch officials are civil servants with almost lifetime tenure. While high-level appointees, such as the EPA Administrator, are at some risk if they make poor decisions, tenured civil servants are not. Citizens who feel aggrieved as a result of executive branch decisions have little opportunity for redress (222).

Field (120) cites a number of legal scholars who contend that "vague mandates" such as TSCA's directions to reduce or eliminate "unreasonable risks" give too much discretion to agencies:

> If regulatory decisions are to be broadly acceptable, the governing statutes must do more

> than provide for decisions about what is safe or what is an unreasonable risk. They must also do more than merely list factors to be considered. The legislative process must make the basic value judgments and tell the agencies how to make the necessary trade-offs. . . .
>
> Insofar as statutes do not effectively dictate agency actions, individual autonomy is vulnerable to the imposition of sanctions at the unruled will of executive officials, major questions of social and economic policy are determined by officials who are not formally accountable to the electorate, and both the checking and validating functions of the traditional model are impaired (120).

Baram (19) draws attention to the frequent absence of confessional direction about what factors agencies are to consider in reducing risk. Absence of that direction, he says, causes the agencies to face extensive litigation.

Judiciary Branch Decisions

Markey (222) expresses concern about the judiciary becoming too involved in making decisions about acceptable risk. He sees such decisions as best made in the political arena by officials responsible to the electorate. Judges, he points out, often enjoy lifetime tenure and are more removed from the electoral process than are executive branch officials.

Vague definitions such **as** "unreasonable risk" that occur in the balancing laws are seen as inviting legal challenge and judicial involvement in risk decisions. The courts have generally given great weight to "agency procedural safeguards, substantiality of evidence, and consistency" **(120),** but two recent developments may alter such preference. As discussed above, the Bumpers amendment would erase the judicial preference shown to agency expertise, and the courts would entertain challenges to agency expertise. Judicial involvement is also increased because of industry challenges to agency rules and consumer, environmental, and labor organization challenges to agencies for not regulating. Whatever the source of challenge, judicial reviews have an impact on what level of risk will be acceptable. Should a court modify an agency-decided risk level, it is reasonable to assume that the agency, in making its next decision, will consider the courts' decree.

Directions From Congress

Congressional attention to details about what to balance and how to balance **are seen as solu**tions to some of the problems of the regulatory agencies. Interestingly, regulatory agency attorneys interviewed by Field (120) generally favored balancing laws. They see their agencies well able to do an adequate job of balancing risks and benefits and evidently do not share the concerns about vague mandates.

Attorneys for four environmental interest groups were also interviewed (120). Three were opposed to balancing laws and favored that the Congress impose clearer mandates for regulatory action. Vague, balancing laws were seen as favoring industry because of its greater resources for influencing decisions in the agencies and in the courts. The fourth environmental attorney suggested that lack of money hampered public interest group representation and that Federal funding for preparation of their cases would ease their difficulties.

Clearly, different laws impose different standards, and the balancing laws are not specific about what is to be balanced. Litigation results from these characteristics of the laws. Congressional intervention to define standards and to detail what to balance should reduce litigation from those sources.

However, there is no guarantee that clearer directions from Congress will eliminate litigation—e.g., FDA's banning of the artificial sweetener, cyclamate, begun in **1969, was con**tested until 1980 (and may be reopened). Of all the carcinogen laws, the Delaney clause, which was the basis of the cyclamate ban, provides the clearest definition of a carcinogen, and it is the simplest in the sense that it allows no balancing. Nevertheless, administrative law hearings contesting the quality of the evidence about carcinogenicity were held off-and-on for a decade. The FDA decision was upheld.

Congress cannot engage in the day-to-day business of agencies; it does not have the time. It

must delegate authority to the agencies. If it shares the opinions of some observers that it does not Provide sufficient direction to the agencies about acceptable risk and balancing, it might provide the direction or it might more often exercise its right to intervene in regulatory activities.

Some risks are inherent in either remedy. Overly strict directions, which provide many points for judicial review might so encumber the agencies that no preventive regulatory action is possible. On the other hand, Congress cannot intervene too often in regulatory matters without hobbling its capacity to deal with other issues.

Regulations are seen as too burdensome by some and too weak by others, but the *regulations* are required by law. The laws are congressional expressions that public policy requires a certain level of protection for public health.

REGULATED CARCINOGENS

Table 38 lists 102 substances and categories of substances regulated under the laws discussed above. In every case, some evidence existed to indicate that the substance is a carcinogen. In many cases, evidence about the substance was generated in the NCI bioassay program (146) and/or evaluated by IARC (185,186). The left-hand columns of the table describe what conclusions were drawn about the human and animal substances by NCI and IARC.

IARC has classified 18 substances or processes as human carcinogens and another 18 as probable human carcinogens. The data in table 38 show that 20 of those chemicals are regulated. Each of those 20 is identified by a "C," carcinogen or "PC" probable carcinogen, in the "H," human evidence, column under IARC.

About one-third of the chemicals tested by NCI or reviewed by IARC present "sufficient" evidence to conclude that they are carcinogens in animals and they can therefore be assumed to present a carcinogenic risk for humans (see, e.g., 185). Chemicals from those classes are indicated with an "S" on the table in the "A," animal evidence, column; the "I" classification means the available evidence is limited but presents a strong warning of carcinogenicity.

About half of the chemicals reviewed by IARC and/or tested by NCI presented neither sufficient nor limited evidence of carcinogenicity. Only one chemical for which there is only inadequate (I) evidence of carcinogenicity appears in table 38. It is not possible to decide from the data in the table that risky chemicals are being regulated at the proper pace, but the data do lead to the conclusion that nonrisky chemicals (as judged by IARC and NCI) are not often regulated. The conclusion then suggests that regulations are not so haphazardly drawn as to regulate large numbers of chemicals that present no or very little risk.

The absence of an entry under "NCI" or "IARC" does not necessarily mean that there is poor or limited evidence about carcinogenicity. For instance, although the first substance, 2-acetylaminofluorene, does not occur on either the NCI or the IARC list, it is an accepted animal carcinogen (see ch. 5). Furthermore, other chemicals have been reviewed since the IARC (186) publication, but the results of the reviews are not yet available.

Some complexities of regulating carcinogens are demonstrated by the table. Some substances present a risk in locations covered by different laws, and separate regulations are necessary for each exposure. Under CAA, EPA has proposed regulation for, or regulated, 6 carcinogens and is considering an additional **24.** Section 311 of CWA deals with oil and hazardous spills, and is not focused on regulating carcinogens, but "hazardous discharge reporting levels" have been promulgated for the listed chemicals, and carcinogenicity was considered in setting those levels. The 49 substances for which regulation is required under section 307 of CWA were included in the law in 1977. Standards have been set for trihalomethanes, including chloroform, under the Safe Drinking Water Act. A few

Table 38.-Substances Regulated as Carcinogens Under Various Acts

Evaluation by NCI	Evaluation by IARC			Statutes							
A	H	A	Chemical	CAA	CWA $307	CWA $311	SDWA	FIFRA	OSHA	FDCA	CPSA
—	—		2-acetylaminofluorene (2-AAF)	—		—	—	—	OSHA	—	—
—	Pc	;	Acrylonitrile	C	RR	L	—	V	R	—	—
—	Pc	S	Aflatoxin	—	—	—	—	—	—	R	—
L	—		Aldrin	—	RR	L	—	V		—	—
—	C	;	4-aminobiphenyl	—		—	—	—	i	—	—
r —	—	S	Aramite	—		—	—	V	—	—	—
—	C	I	Arsenic	P	RR	—	R[a]	R	R	—	—
—	C		Arsenic compounds	—	RR	L	—	R	—	—	
—	C	i	Asbestos	R	RR	—	—	—	R[a]	—	i
—	—	S	Benz(a)anthracene	—	RR	—	—	—	.—	—	—
—	C	A	Benzene	P	RR		—	—	R	—	R
—	C	A	Benzidine	—	RR	L	—	—	R	—	R
—	—	S	Benzo(b)fluoranthene	—	RR	—	—	—	—	—	—
—	—		Benzo(a)pyrene	C	RR	—	—	—	—	—	—
—	Pc	:	Beryllium	R	RR	—	—	—	. -	—	—
—	Pc	S	Beryllium compounds	—	RR	L	—	—	—	—	—
—	—	L	Bis(2-chloroethyl)ether (BCEE)	—	RR	L	—	—		—	—
—	C	s	Bis(chloromethyl)ether (BCME)	—	RR	—	—	—	R	—	—
—	Pc		Cadmium	C	RR		R[a]	R	—	—	—
—	I	:	Cadmium compounds	—	RR	L	—	R	—	—	—
—	I	s	Carbon tetrachloride	C	RR	L	—	—	—	—	—
S	I	L	Chlordane	—	RR	L	—	R	—	—	—
S	—	L	Chlorobenzilate	—	—	—	—	R	—	—	—
S		s	Chloroform (a trihalomethane, THM)	C	RR	L	R	—	—	—	—
—	c	s	Chloromethyl ether	—	—	—	—	—	R	—	—
—		s	Chromium compounds (hexavalent)	—	RR	L	—		—-	—	—
—	c	s	Coal tar and soot	—	—	—	—		—	—	—
—	—	N	Coke oven emissions (polycyclic organic matter; "POM")	C	—	—	—	—	R	—	—
—	—	N	Creosote	—	—	—	—	R	—-	—	—
—	—	N	Cyclamates	—			—	—	—	R	—
—	—	N	D&C Blue No. 6	—	—	—	—	—	—	R	—
—	—	N	D&C Red No. 10	—	—		—	—	—	R	—
—	—	N	D&C Red No. 11	—	—	—	—	—	—	R	—
—	—	N	D&C Red No. 12	—	—	—	—	—	—	R	—
—	—	N	D&C Red No. 13	—	—	—	—	—	—	R	—
—	—	N	D&C Yellow No. 1	—	—	—	—	—	—	R	—
—	—	N	D&C Yellow No. 9	—	—	—	—	—	—.		—
—	—	N	D&C Yellow No. 10	—	—	—	—	—	—	:	—
—	I		DDT (dichlorodiphenyltrichloroethane)	—	RR	L	—	R	—	—	—
—	—	:	Dibenz(a,h)anthracene	—	RR	—	—	—	—	—	—
S	—	s	1,2-dibromo-3-chloropropane	—	—	—	—	R[a]	R	—	—
—	—	N	1,2 dibromoethane	C	—	L	—	R	—	—	—
—	—	s	3,3' -dichlorobenzidine	—	RR	L	—	—	R	—	—
S	—	s	1,2-dichloroethane	C	RR		—	—	—	—	—
I	i	L	Dieldrin	—	RR	L	—	R	—	—	—
—		N	Diethyipyrocarbonate	—	—	—	—	—	—	R	—
—	c	s	Diethylstilbestrol (DES)	—	—	—	—	—	—	R	
—	—		4-dimethylaminoazobenzene	—	—	—	—	—	R	—	
L	—	:	2,4-dinitrotoluene	—	RR	L	—	—	—	—	—
S	—	s	1,4-dioxane	C	—	—	—	—	—	—	—
—	—	N	1,2-diphenylhydrazine	—	RR	L	—	—	—	—	—
—	—	L	Dulcin	—	—	—	—	—	—	R	—
—	I	L	Epichlorohydrin	C	—	L	—	—	—	—	—
—	—	N	Ethylene bis dithiocarbamate	—	—	—	—	R	—	—	—
—	Pc	I	Ethylene oxide	C	—	—	—	R	—	—	—
—	—	N	FD&C Red No. 2	—	—	—	—	—	—	R	—
—	—	N	FD&C Violet No. 1	—	—	—	—	—	—	R	—
—	—	N	Formaldehyde	C	—	L	—	—	—		—
—	—	N	Graphite	—	—	—	—	—	—	i	—
(S)	—	L	Heptachlor	—	RR	L	—	R	—	—	—
—	—	s	Hexachlorobenzene	—	RR	L	—	—	—	—	—
—	—	N	Hexachlorobutadiene	—	RR	L	—	—	—	—	—

Table 38.–Substances Regulated as Carcinogens Under Various Acts (Continued)

Evaluation by NCI	IARC			Statutes						
A	I - f	A	Chemical	CAA	CWA $307	CWA $311	SDWA	FIFRA	OSHA	FDCA	CPSA
—	I	L	Hexachlorocyclohexane	—	—	L	—	—	—	—	—
—	—	N	a-hexachlorocyclohexane	—	RR	L	—	—	—	—	—
—	—	N	β-hexachlorocyclohexane	—	RR	L	—	—	—	—	—
(S)		N	Hexachloroethane	—	RR	L	—	—	—	—	—
	—	S	Ideno(1 ,2,3-cd) pyrene	—	RR	—	—	—	—	—	—
S	—	S	Kepone (chlordecone)	—	—	L	—	V	—	—	
—	—	L	Lindane	—	RR	L	R[a]	R	—	—	—
—	—	N	Mercaptoimidazoline	—	—	—	—	—	—	R	—
—	—	S	4,4' methylene bis (2-chloroaniline)	—	—	—	—	—	R	R	—
—		L	a-naphthylamine	—	—	—	—	—	R	—	—
—	c	S	2-naphthylamine	C	—	—	—	—	R	—	—
—	Pc	S	Nickel	C	RR	—	—	—	—	—	—
—	Pc	S	Nickel compounds	—	RR	L	—	—	—	—	—
—	—	N	Nitrosamines	—	—	—	—	—	—	R	—
—	—	L	4-nitrobiphenyl	—	—	—	—	—	R	—	—
—	—	S	N-nitrosodi-n-butylamine	—	—	L	—	—	—	—	—
—	—	S	N-nitrosodiethylamine (DENA)	—	—	L	—	—	—	—	—
—	—	S	N-nitrosodimethylamine (DMNA)	C	RR	L	—	—	R	—	—
—	—	S	N-nitrosodi-n-propylamine		RR	—	—	—	—	—	—
—	—	S	N-nitroso-N-ethylurea (NEU)	;	—	—	—	—	—	—	—
—	—	S	N-riitroso-N-methylurea (N MU)	C	—	—	—	—	—	—	—
—	—	N	Oil of calamus	—	—	—	—	—	—	R	—
—	—	N	P-4000	—	—	—	—	—	—	R	—
I	—	N	Pentachloronitrobenzene(PCNB)	—	—	—	—	R	—	—	—
—	I	S	Polychlorinated biphenyls (PCBs); Toxic Substances Control Act-RR)	C	RR	L	—	—	—	R	—
—	—	S	p-propiolactone	—	—	—	—	—	R	—	—
—	—	S	Safrole	—	—	—	—	v	—	R	—
—	—	N	2,3,7,8 -tetrachlorodibenzo-p-dioxin (TCDD, "dioxin")	C	RR	—	—	—	—	—	—
(S)	—	N	1,1 ,2,2 -tetrachlorethane	C	RR	L	—	—	—	—	—
(S)	—	N	Tetrachloroethylene (perchloroethylene)	C	RR	L	—	—	—	—	—
—	—		Thiourea	—	—	—	—	—	—	R	—
(S)	—	:	Toxaphene	—	RR	L	R[a]	R	—	—	—
(S)	—	N	1,1 ,2-trichloroethane		RR	L	—	—	—	—	—
(S)	I	L	Trichloroethylene	C	RR	L	—	—	—	—	
S	—	N	2,4,6-trichlorophenol	—	RR	—	—	—	—	—	
—	—	N	Trihalomethanes (THM)	—	—	—	R	—	—	—	—
—	—	N	"Tris" (flame retardant)		—	—	—	—		—	R
—	c	S	Vinyl chloride	G	RR	—	—		k	—	R
—	—	N	Vinylidene chloride	C	RR	L	—	—	—	—	—
—	—	—	Radionuclides	R	—	—	—	—	—	—	—

Abbreviations

NCI National Cancer Institute data (146)

IARC International Agency for Research on Cancer evaluation (185. 186)
- A = animal evidence
- S = sufficient evidence for carcinogenicity (for more description see Chapter 4, Appendix A)
- (S) = Class 3 of NCI; very strong evidence is 1 species; no evidence in 2nd species
- L = limited evidence for carcinogenicity
- I = inadequate evidence for carcinogenicity
- H = human evidence
- C = identified as a carcinogen from human studies
- PC = identified as a probable carcinogen from human studies
- I = inadequate evidence to reach a conclusion about carcinogenicity from human studies
- N = not evaluated

CAA Clean Air Act
CWA 307 Clean Water Act &307
CWA 311 Clean Water Act 31 1
SDWA Safe Drinking Water Act
FIFRA Federal Insecticide, Fungicide, and Rodenticide Act
OSHA Occupational Safety and Health Act
FDCA Food, Drug, and Cosmetic Act
CPSA Consumer Product Safety Act

- C = being considered for regulation
- P = regulation proposed
- R = regulated
- RR = regulation required by Act
- L = discharge levels restricted
- v = voluntarily withdrawn from market

aRegulation based on non-carcinogenic toxicity (in addition to those indicated, many other listed substances encountered in the workplace are regulated because of toxicities other than carcinogenicity).

metals and pesticides which are identified as carcinogens are regulated under the same act but because of other toxic properties. Implementation of FIFRA has resulted in voluntary withdrawal of pesticides before regulations were promulgated as well as regulations restricting or forbidding use.

OSHA has regulated the substances shown because of carcinogenicity and many other substances on the list are regulated in the workplace because of other toxicities. FDA regulation of carcinogenic food additives and colors has eliminated most of the listed colors and sweeteners from the food supply. The Consumer Product Safety Commission has regulated five chemicals and benzidine-containing dyes.

The table does not discriminate between regulations that set a permissible limit, such as the OSHA standards, and those that ban a substance, such as FDA regulations of food colors. The entry "R" indicates only that some regulation is in effect.

The laws are designed to reduce exposure to carcinogens. They may regulate too many or too few chemicals, but chemicals are being regulated. Furthermore, apparently, few nonrisky chemicals have been regulated under the current system.