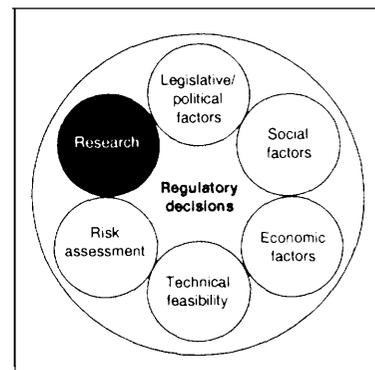


Setting Priorities for Risk Assessment Research

4

Congressional mandates for risk reduction, the public's desire for health and safety, and court rulings requiring justification of health-based regulatory actions have increased pressure to provide ever greater scientific underpinnings for health risk assessments. Judged by the rate of change in risk assessment methodology and the controversies that surround risk assessment, Federal agencies lack the necessary resources to meet that demand and can only support a portion of the research that could or would be useful to them. This chapter examines how Federal agencies determine their priorities for health risk assessment research, that is, the type or types of research an agency will support and conduct. For this analysis, the Office of Technology Assessment (OTA) categorized such research as methodological, basic, or chemical-specific data development.

Priority-setting is influenced by factors that operate at the national, agency, or programmatic levels. The impact of national goals on individual projects or, conversely, the effect of individual projects on national goals, is difficult to gauge, but generally one can expect that effects at one level will reverberate to another. For example, the acquired immunodeficiency syndrome (AIDS), became a national concern, and more resources were directed toward understanding the disease, which resulted in greater participation by scientists from different disciplines in the research. The influx of talent and resources affected the nature of the approaches used to combat the disease and also contributed to research in other fields (U.S. Congress, OTA, 1990).¹



¹ See Joseph (1992) for a discussion of the role of politics in setting the scientific and public health priorities for AIDS research and treatment.

CATEGORIZING HEALTH RISK ASSESSMENT RESEARCH

The types of research that Federal agencies conduct to improve health risk assessments can be categorized using several different approaches. One approach is the traditional division between basic and applied scientific research (Merton, 1973). That approach would distinguish research focused on, expanding knowledge about human diseases and their relationships to environmental factors from research more directly linked to regulatory agendas.

Basic or pure science involves studies “ordered around the expansion of knowledge and competence without any regard for practical application” (Barnes and Edge, 1982). For health risk assessment, this kind of research usually occurs within well-defined disciplinary boundaries—for instance, genetics, molecular biology, chemistry—and involves testing explanatory hypotheses (e.g., about the normal and abnormal functions of organ systems or mechanisms of carcinogenesis) with a variety of experimental methods.

Applied science, in contrast, focuses on increasing and improving “the stock of existing practically useful techniques, processes, and artifacts” (Barnes and Edge, 1982). It involves developing information that may be useful for resolving outstanding practical questions (Lindblom and Cohen, 1979). For health risk assessment, those questions are usually determined by the management problems that regulatory agencies confront (e.g., should human exposure to air pollution be reduced?), and they require interdisciplinary efforts to characterize the pros and cons of taking action. Applied research in health risk assessment can involve experimentation that also contributes to basic scientific understanding, but its predominant motivation is to provide a basis for regulatory decisionmaking.

There are two broad subcategories of applied research in health risk assessment: 1) substance-specific investigations, e.g., conducting toxicity tests or monitoring exposures; and 2) methodo-

logical research that can improve either qualitative or quantitative risk assessment techniques, e.g., developing new testing methods or new low-dose extrapolation models.

Although these categories of risk assessment research are useful for characterizing the activities of Federal agencies, they are not absolute because the boundaries between basic and applied research are frequently blurred. Neurotoxicity testing, for example, can contribute to a basic understanding of neurobiology even as it produces results that are useful for identifying neurotoxic agents for regulatory purposes. Similarly, basic scientific findings, such as the discovery of oncogenes, have important implications for applied research on chemically induced cancers.

Both sociologists of science and regulatory policy analysts have developed their own approaches to categorizing risk assessment research. If one focuses on why research is undertaken and on the standards used to evaluate its results, it is possible to distinguish between *normal* (Rushefsky, 1986) and *mandated* (Salter, 1987), or *regulatory* (Jasanoff, 1990), science.

In *normal* science, researchers conduct investigations as part of a basic research program (Lakatos, 1978), and results are evaluated on the basis of their reproducibility and the contribution they make to resolving outstanding scientific questions. The standards of proof for accepting findings are quite rigorous because scientists are reluctant to mistakenly assert that relationships exist—for example, between a chemical exposure and human cancer—when such relationships might in fact be due to chance (Cranor, 1993).

In contrast, *mandated* science is conducted in response to statutory mandates—instructions to regulatory agencies to identify potential health hazards and control exposures to them to prevent human illness. The results of research conducted within that kind of institutional environment are evaluated against a broader set of criteria than is typical of normal science and frequently involve standards of proof that can conflict with the standards of basic research science (Clark and

Majone, 1985; Jasanoff, 1989). Findings that indicate potential risks to human health, for example, will be judged not only on the basis of the standards of normal science but also on the basis of regulatory standards. If a regulatory agency concludes that a risk is present and if opportunities are at hand to prevent a public health problem, regulatory action may be taken on the basis of less-than-conclusive scientific evidence.

Science used in policymaking can be broken down further into three basic types of activities: knowledge production, knowledge synthesis, and prediction (Jasanoff, 1990). Knowledge production takes in research that is conducted to fill gaps in the information base relevant to regulation; an example would be toxicity testing. Knowledge synthesis involves collecting, evaluating, and characterizing the available scientific information about potential environmental problems and often results in comprehensive risk assessment reports. The most contentious aspect of regulatory science involves predicting the health risks posed by exposure to different toxic agents. Prediction usually depends on a variety of models and assumptions that bridge the gaps between current scientific understanding of relationships between exposure to toxic agents and health outcomes and a projection of what relationships might exist under different conditions.

Because all of these activities are oriented toward resolution of questions on policymaking, a characteristic feature of mandated science is the extensive involvement of nonscientific institutions, such as Congress, the courts, and the media, in the process of producing and certifying knowledge. In that political environment, normal science's approach to reducing uncertainty (conducting further research) is frequently unsatisfactory, because decisions to wait are often interpreted as decisions not to act to protect public health.

Although the distinction between normal and mandated science cannot easily be used to classify the research activities of Federal agencies, it

nevertheless illuminates a number of current policy debates about the appropriate focus of scientific research conducted by regulatory bodies. The results of agency research programs are sometimes evaluated by using criteria from basic science; that practice may lead critics to conclude that the products of agency research are deficient and that increased attention to basic research is necessary to produce "credible" science (U.S. EPA, 1992). An example is the controversy over testing priorities at the National Toxicology Program (NTP). From a normal science perspective, rodent bioassays should be conducted as part of a research program to discover basic mechanisms of toxicity and to define the relevance of positive results in animal tests for assessing the risks to humans. But from the perspective of mandated science, bioassays are part of a large-scale screening effort to identify potential chemical hazards in the environment. Increased attention to studying mechanisms for determining human relevance means that fewer chemicals are screened and that exposure to avoidable causes of human disease is potentially greater.

Another approach to categorizing risk assessment research is by examining the potential for new scientific investigations to increase the knowledge base and decrease policy conflicts. A simple model developed by policy analysts categorizes the results of research along two dimensions: the extent to which they contribute to scientific knowledge and the extent to which they increase or decrease policy conflict (Graham et al., 1988). This perspective on the contributions of health risk assessment research is clearly helpful for establishing priorities and formulating a national research agenda. Investments in research that contribute to the knowledge base and reduce policy conflict are clearly optimal. But because of the way science works, results may uncover new conflicts that require additional experimentation well beyond what can be accomplished with available techniques. Case studies of U.S. regulatory policy regarding carcinogens have concluded that more research, leading to

more knowledge, does not necessarily result in less policy conflict. Extensive investigations of the mechanisms by which formaldehyde causes cancer in rodents, for example, have raised more questions about the possibility of low-dose risks to humans than they have answered. The result is an increase rather than a reduction in policy conflict (Graham et al., 1988).

These analytical perspectives on the different rationales for conducting basic and applied research on risk assessment and on the varied effects that research can have on the knowledge base and the policy process are essential for a balanced assessment of current efforts by Federal agencies. Scientific optimists, for example, might look at the tremendous advances being made in molecular biology, and conclude that support for that research is more worthwhile than support for less scientifically interesting programs of toxicity screening. But the results of basic science research may not be immediately applicable for regulatory decisions. There is clearly a need for applied research to provide data for preliminary determinations about possible hazards before acquiring a complete understanding of the hazard. Similarly, there is a need to develop risk assessment methodologies that address the inevitable gaps in scientific understanding in order to characterize potentially significant risks to health. However, to the extent that uncertainties are ever reduced, the reduction is more likely to come from an integration of basic and applied research.

To narrow its range of inquiry, OTA restricts risk assessment research to two types of activities:

1. Generalizable research to improve methods for assessing the risks of adverse health effects from food contaminants and environmental and workplace exposures, and
2. Research to improve estimates of risks from exposure to specific agents.

Because of the controversies surrounding the methods for evaluating and estimating risks from

exposure to agents suspected of causing cancer, this report frequently uses research to improve the assessment of risk from potential carcinogens to illustrate the directions and needs of research on health risk assessment in general.

Given that framework, OTA divided health risk assessment research into three key areas (table 4-1). Two of the areas encompass more general research, and the third encompasses chemical-specific research. Methodological research, the first area, is specifically aimed at improving the approaches and methods used for assessing risks. The second, basic research, contributes to an understanding of how environmental agents perturb normal biological functioning. The third category involves research that expands the database about specific chemicals for use in risk assessments. The results of all three types of research are crucial; inadequate development in any one area could impede progress toward the overarching objective of making risk assessment more credible and its results more widely accepted. For instance, the models developed in methodological research depend on the results of basic research and chemical-specific data development.

OTA used these classifications as a better representation of research activities than the process of risk assessment outlined by the National Research Council (NRC) in 1983 (NRC, 1983). As discussed more fully in chapter 2, NRC's sequential four-step process begins with hazard identification, progresses to dose-response and exposure assessments, and ends in risk characterization. The NRC "paradigm" laid out and formalized the risk assessment process and made it transparent for decisionmakers and the public alike, but it does not delineate the different kinds of research that underpins each step (Paustenbach, 1989; Rosenthal et al., 1992). OTA's analysis focuses on three distinct objectives of health risk research: improving health risk assessment methodologies, understanding how environmental agents produce their adverse effects, and filling chemical-specific data gaps.

Table 4-I-Categories of Health Risk Research

Methods Development

Method and model development—Developing tests and structure-activity analysis for identifying toxicants; developing models for predicting human exposures; developing methods for extrapolating effects, dose, and dose-response from laboratory study results to humans. Activities for method and model development include:

- . Toxic effects identification and extrapolation
- . Exposure extrapolations
- * Dose-response extrapolations
- . Uncertainty analysis

Methods evaluation and validation—The iterative process for validating new methods by comparisons to methods of known and established veracity. When validated, methods can be applied to risk assessments.

Basic Research

Toxicity mechanisms—Research to determine the nature, sequence, and combinations of events that result from exposure of test animals or humans to toxicants. This includes the study of the concentration of the toxicant or its metabolize that reaches the site of action, the rates and nature of the reactions with target organs or tissue that are causally linked to disease or the development of toxic effects, and an understanding of how the toxic effect comes about.

Biological and biomedical—Research on the structure and function of molecules, cells, organs, physiological systems, and organisms. The resulting knowledge of comparative genetics, biochemistry, and physiology can be used to guide studies on toxicity mechanisms or reduce uncertainty in effects, dose, and dose-response extrapolations.

Chemical and physical sciences—Research on physical and chemical properties that govern absorption, distribution, fate, transport, and transformation in the environment and in biological systems.

Chemical-Specific Data Development

Toxic effects—Research designed to identify the toxic effects of agents and the nature of dose-response relationships under defined conditions of exposure. Activities include:

- . Human studies
 - Whole-animal studies
 - Mammalian tissue, organ, and cellular studies
- . Microorganism and other studies

Human exposure data—Measuring toxicant levels in different media or commodities and biological materials to test predictive models and to validate measurement methods.

SOURCE: Office of Technology Assessment, 1993.

Research to Improve Health Risk Assessment Methods

OTA sees the goal of research on health risk methodology as development of better methods for extrapolating results: from animal models to humans, from high to low exposures, and from emission data to predictions of population or individual exposure. It also encompasses efforts to estimate uncertainty and develop new methods for toxicity testing. An important and often overlooked part of methods research is evaluating and validating the methods with experimental data.

Many scientists argue that methodological research holds the most immediate promise for substantive improvement of risk assessments.

To begin with, generic methodology research, in contrast to chemical-specific studies, can have considerable impact on assessing the risks from exposure to many different chemicals and radiation. Moreover, when the methods are directed at the most uncertain aspects of risk assessments (extrapolations from high to low doses and from animal models to human populations and predicting the risk of chemicals for which few or no toxicity data exist), they can reduce the range of uncertainties in current risk assessment approaches. Because of a number of characteristics, methodological research falls in between basic and chemical-specific research, making it a bridge between basic and applied efforts. In other respects,

however, this research is sufficiently unique that its practitioners refer to it as “risk science.”

Basic Research To Support Risk Assessment

For the purposes of this report, basic research is separated into two types: basic health risk research and basic sciences research. Basic health risk research investigates the mechanisms of disease associated with exposure to toxic agents. These studies examine the fate and transport of chemicals and physical agents, the avenues of exposure, and interactions with living systems and biological tissues, all of which feed into health risk assessment research. The focus of basic health risk research on the application of results to risk assessment problems and opportunities sets it apart from the basic sciences.

Basic sciences research encompasses the basic biological and biomedical, chemical and physical sciences. Although some research in the basic sciences contributes to risk assessment research, basic sciences research is a very broad endeavor, and it is not included in OTA’s analysis of relevant research. These studies examine the structure and function of molecules, cells, organs, and physiological systems and their relationship to the functioning organism, as well as the properties of chemicals and physical agents.

Of the three types of health risk assessment research, findings from basic research usually require the most time to be incorporated into decisionmaking. The research has also been generally characterized as having the lowest probability of success. Nevertheless, it can serve as the foundation for developing new methods in generating or applying primary data for health risk assessment and affect risk assessment in a far-reaching way, as it does other applications of science. Recently, techniques and findings from basic research have been rapidly incorporated into health risk research. Within the past several years, for example, many molecular biological

principles and techniques have proliferated throughout the field of toxicology (Olden, 1993).

Chemical-Specific Data Development

Chemical-specific data development identifies the toxic effects of agents and characterizes dose-response relationships under defined conditions of exposure. Efforts to identify toxicants probably constitute the broadest and most diverse type of data development. Usually, they involve testing agents in laboratory animals, sometimes complemented by results from epidemiologic studies. This type of research also includes collecting data on exposure of humans to environmental agents. Some scientists dismiss the idea that collecting or gathering data using “routine” tests or monitoring methods is research. In contrast, the majority of scientists who advised OTA in the study and who reviewed drafts of this report voiced the opinion that such activities are properly classified as research. In OTA’s evaluation of research funding, only two Federal agencies reported collection of exposure data as a research activity, but many included toxicity testing in research activities. The programs that carry out toxicity tests do more than provide the basic information for risk assessments, they also do research that leads to better tests and basic research on mechanisms of disease causation.

A look at the number of existing chemicals and the new compounds that appear each year explains the need for further toxicity testing and data development. Since 1965, more than 12 million chemicals have been entered into the Chemical Abstract Service’s registry file (although the actual number of chemicals to which individuals might be exposed is considerably smaller). The reporting provisions of the Toxic Substance Control Act require an inventory of the chemicals currently being manufactured in this country; that list contains more than 61,000 chemicals (Lao, 1993). More than 3,000 chemicals are registered as pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act, a listing that consists

of 880 active pesticidal ingredients and 2,200 inert ingredients (Colledge, 1993). The number of food additives is 3,151 (Hudson, 1993).

After reconciling for overlaps, OTA estimates that 62,512 chemicals are present in commerce in the United States. A recent gathering of environmental experts estimated that “good” data on the health effects from exposure are available for only 10 percent of chemicals existing worldwide, with nearly 1,500 being developed each year (Environmental Health Letter, 1993).

FEDERAL RESOURCES FOR HEALTH RISK ASSESSMENT RESEARCH

The Federal Government’s support for research on health risk assessment extends from basic studies in the biological and biomedical sciences to methods for extrapolating observations from one setting to another. That breadth was evident during OTA’s attempts to evaluate the resources devoted to improving health risk assessment. Under the broadest definition of research that affects health risk assessment, a significant portion of the Federal Government’s obligations in health research and development (R&D) generally can be considered as contributing to the effort.

OTA used the research objectives and the categories of risk assessment research discussed above, which parallel the categories used by the executive branch,² as the framework for the analysis of agency research resources. This analysis used three main sources of information: the 1992 data book of the National Institutes of Health (see app. C); the annual National Toxicology Program (NTP) review of the research related to toxicology (U.S. DHHS, in press), which includes basic toxicology research, epidemiol-

ogic and methodologic research being performed by the Department of Health and Human Services (DHHS) agencies (see app. D), Department of Energy (DOE) and Environmental Protection Agency (EPA); and OTA’s requests to the various agencies for data on resources. OTA also contacted organizations such as the National Science Foundation and the American Association for the Advancement of Science, which have recently completed reports on Federal environmental research. The best of these sources, for the purposes of this report, proved to be the NTP review .

OTA’s call for information from the various Federal agencies resulted in estimates of resources that were highly dependent on how the responder defined health risk assessment research. For example, with a broad definition of research related to health risk assessment, about 33 percent of the 1993 budget of the National Cancer Institute (NCI) or about \$600 million, would be related to this activity (Lee, 1993). But using data from NTP’s review of current research (U.S. DHHS, in press) as representative of their research on health risk assessment, the NCI support would be estimated at \$80 million, or about 4 percent of the 1993 NCI budget. Consequently, OTA concluded that it had not obtained wholly reliable estimates of resources; nonetheless, OTA discerned some general trends and directions.

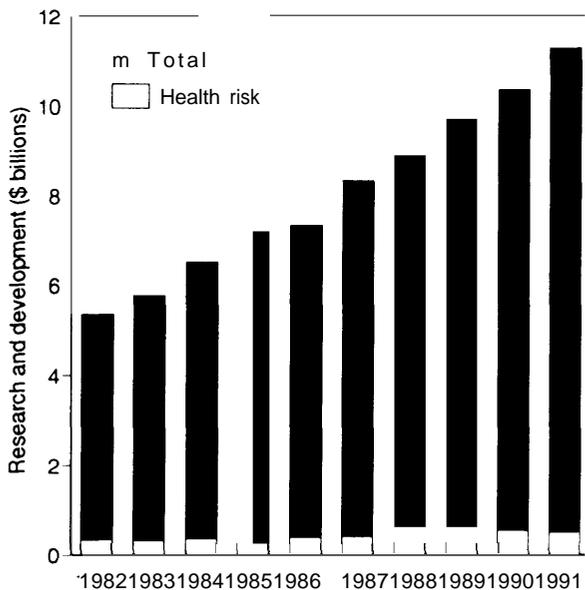
using Summary data issued between 1982 and 1991 from the NTP review of research related to toxicology as a surrogate for health risk R&D,⁴ OTA determined that total support of health risk assessment research increased from \$336 to \$520 million, a 55 percent increase before adjusting for inflation. During the same period, Federal obligations for health R&D, as reported in the National

² The NTP Annual Reviews of Research Related to Toxicology compiles data on agency programs in the Categories of Basic Toxicology Research, Toxicology Testing, and Toxicology Methods Development (U.S. DHHS, in press).

³ The NTP review includes human epidemiology studies as toxicology testing.

⁴ OTA’s survey in 1993 indicates health risk research is also carried out by the Department of Defense, Department of Agriculture, the Consumer Product Safety Commission and Nuclear Regulatory Commission. NTP data did not cover resources for those agencies. However, their contributions are small relative to the agencies covered in the review.

Figure 4-1—Funding for Federal Health Research and Development, Fiscal Years 1982-91



a Total.
b Health risk.

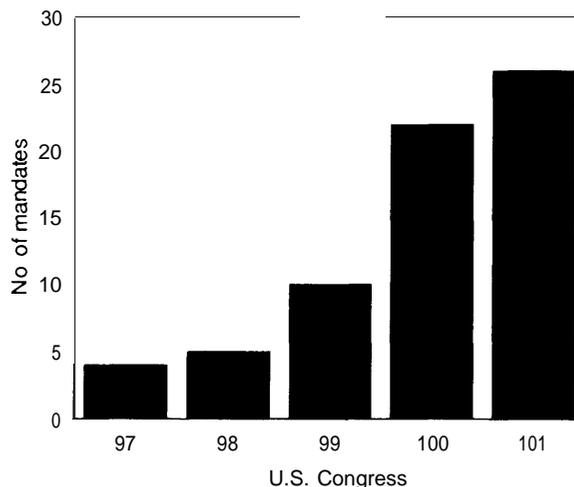
SOURCE: Office of Technology Assessment, based on National Institute of Health Data Book, 1992; and Review of Current DHHS, DOE and EPA Research Related to Toxicology, Fiscal Years 1982 through 1991, National Toxicology Program, U.S. Department of Health and Human Services.

Institutes of Health data book, increased from \$5.0 to \$10.7 billion, a 123 percent increase before inflation (figure 4-1).

With the above data, OTA estimated health risk R&D's share of total Federal health R&D dropped from 6.8 percent in 1982 to 4.9 percent in 1991. Moreover, this relative decline in health risk R&D took place during a period of expanding Federal legislation and responsibilities to protect human health from environmental pollutants. During that period, the number of environmental legislative mandates increased with each successive Congress—4 in the 97th Congress (1981 and 1982) to 26 in the 101st Congress (1989 and 1990) (figure 4-2).

The NTP data describe the funding support for research related to chemical toxicology in methods development, basic toxicology, and testing (data development) (figure 4-3). These data

Figure 4-2—Environmental Legislative Mandates



SOURCE: Office of Technology Assessment, 1993.

represent the research priorities for the three types of health risk research. Of the \$524.8 million spent for the total research effort in fiscal year 1992, methodological research received 15.6 percent, basic research 58.3 percent, and testing 26.1 percent.

In addition the NTP data also illuminated trends in how the various agencies separately apportioned support and resources for those types of research (figure 4-4). In general, over the 1980-92 period, research agencies such as the National Institute of Environmental Health Sciences (NIEHS) and the National Cancer Institute increased the percentage of basic toxicological research that they conducted. In contrast, regulatory agencies such as EPA and the Food and Drug Administration (FDA) devoted a larger proportion of their health R&D to methods research than did the research institutes.

In this figure, the personnel numbers, in full-time equivalents (FTEs), devoted to this research reflect the size of the intramural program. In general, the regulatory agencies have sizable intramural programs compared to their R&D budgets, while the research agencies support relatively larger extramural programs. The number of FTEs at EPA, for example, is nearly

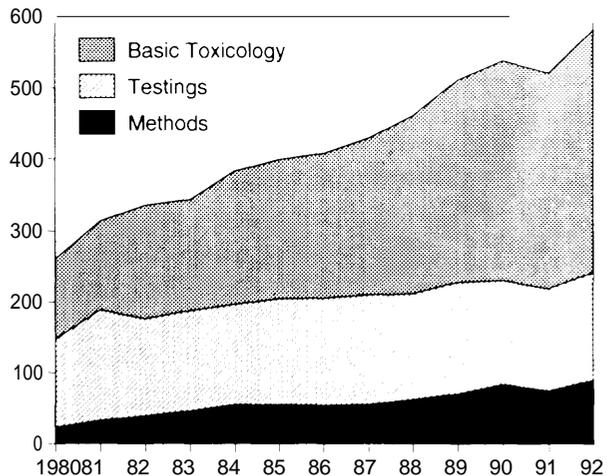
equivalent to NIEHS, but EPA's R&D budget is only about one-third the size.

Taken together, the budget and personnel figures provide a picture of the Federal health risk R&D effort and the priorities of the agencies. To begin with, these data show that NIEHS devotes the most resources, in both dollars and FTEs, to health risk research. Furthermore, the agencies with substantial extramural programs, NIEHS and NCI, to a large extent support basic research. The intramural program at NCI is predominantly basic in nature, whereas it is more evenly distributed at NIEHS among the three types of research. As the graphs in figure 4-4 demonstrate, NCI transferred its carcinogen testing program to NIEHS in 1982. The remaining four programs in this figure operate mostly intramural research programs. As the agencies reported in the NTP Review, EPA and NIOSH programs conduct mostly methodological research, while, at the FDA, the National Center for Toxicological Research's (NCTR) research is mostly basic and the Center for Food Safety and Applied Nutrition's (CFSAN) is more evenly distributed.

Based on fiscal year 1993 estimates in the OTA survey of research (table 4-2A), less than 11 percent (\$65 million) of the total R&D budget of \$600 million for environmental and occupational health and food safety is devoted to research on methods. It is possible only to estimate roughly the total amount that was actually spent on methods research during the period, because of the difficulties in categorizing the research. Nevertheless, the small size of the risk research analysis programs at the NCTR and NIEHS, and the reported part-time participation of researchers at the regulatory agencies, support a conclusion that methodological research is underfunded.

To get a broader accounting of the FY 1992 research resources, OTA incorporated data from the Departments of Defense and Agriculture with the NTP review data (table 4-2B). In table 4-2B, OTA estimates that the agencies devote nearly 16 percent (\$91.6 million) of the total \$589.5 million spent in FY 1992 to methods research. The

Figure 4-3-Federal Research Related to Chemical Toxicology (In millions of dollars)



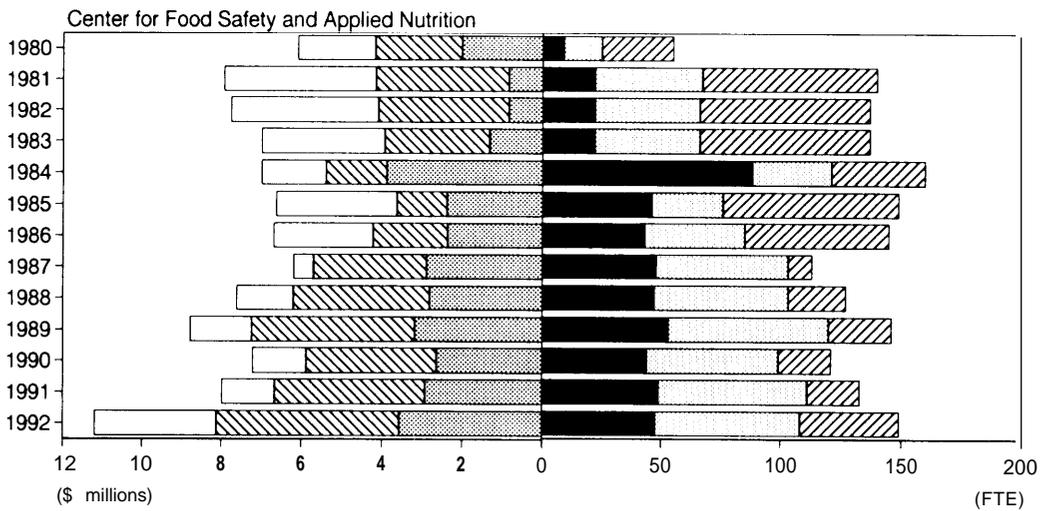
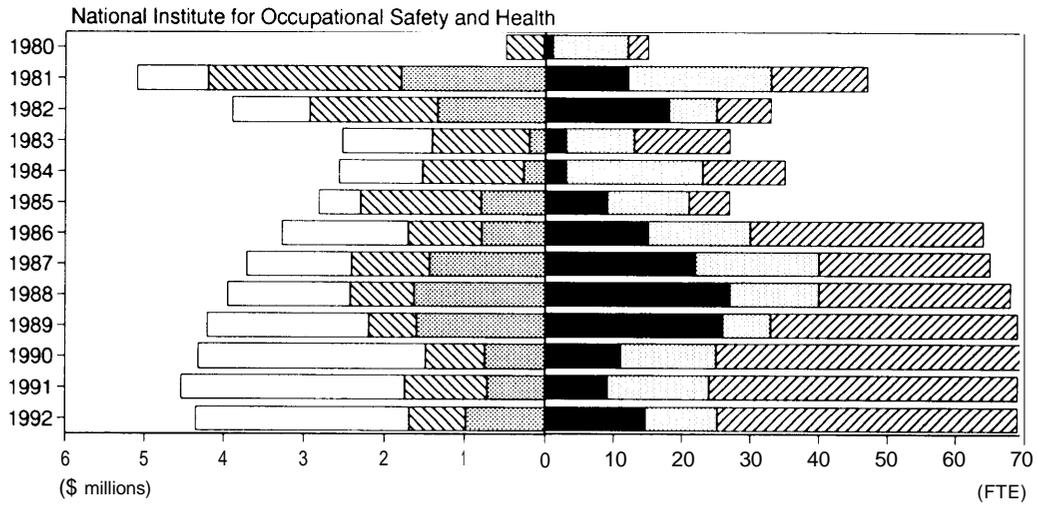
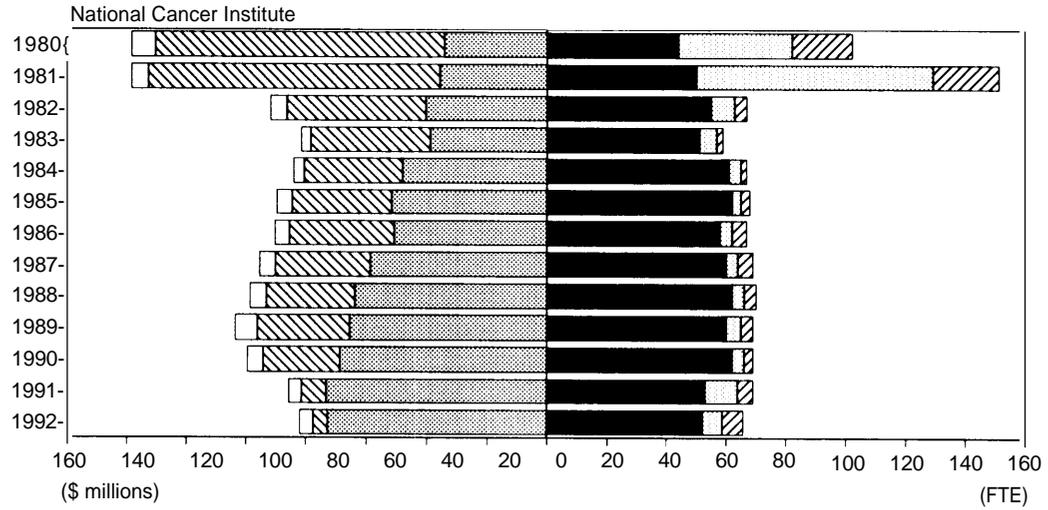
SOURCE: Office of Technology Assessment, 1993, based on data from Review of Current DHHS, DOE and EPA Research Related to Toxicology, Fiscal Years 1980 through 1992, National Toxicology Program, U.S. Department of Health and Human Services.

discrepancy between the 1992 and 1993 figures may result from different reporting methods: OTA based the FY 1993 estimates on the results of its agency survey, whereas the 1992 estimates are based on the results of the 1992 NTP review DHHS, DOE, and EPA research (U.S. DHHS, in press). The differences between the two tables illustrate the difficulties in obtaining accurate resource figures.

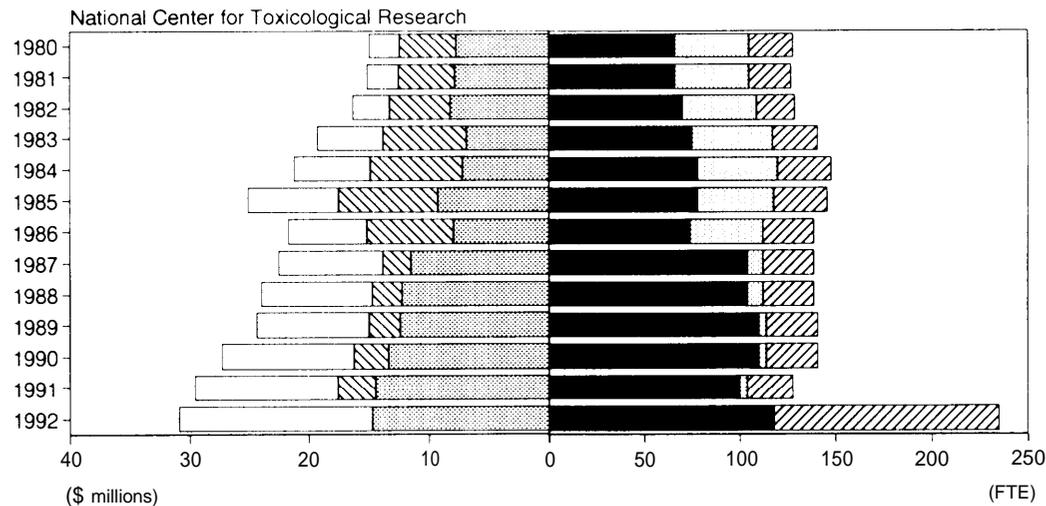
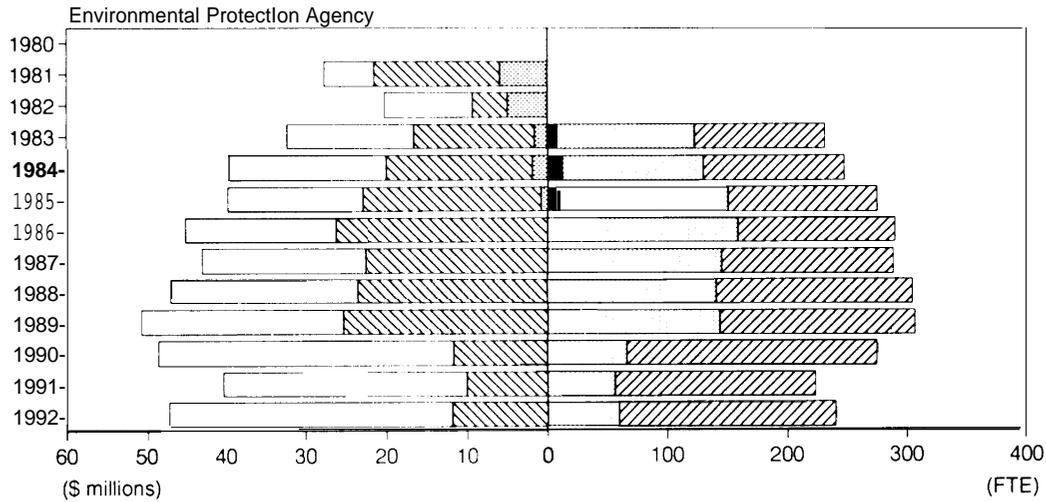
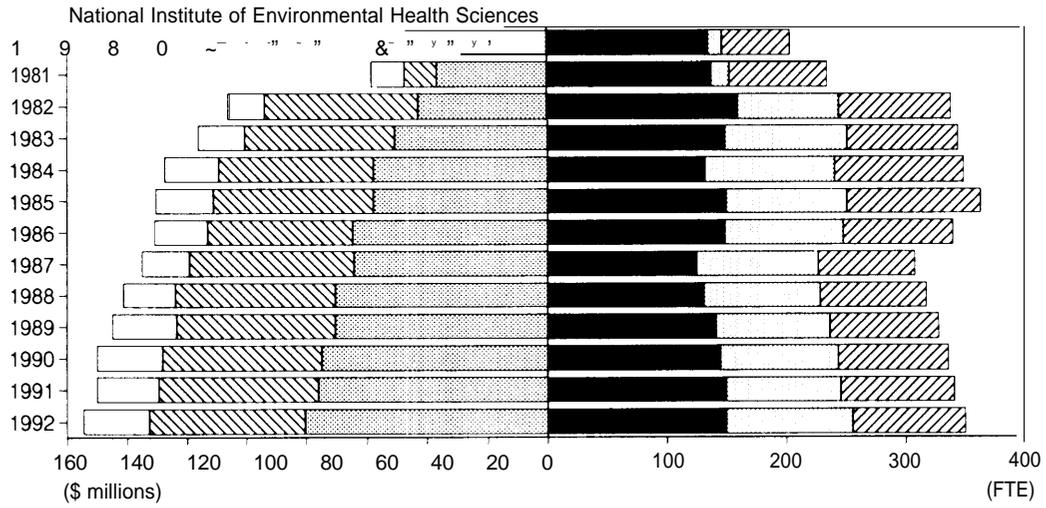
A consistently understudied area is human exposure measurement. Historically, exposure-related research efforts have concentrated on identifying the presence or determining the fate and transport of pollutants in various media. OTA's survey did not cover the entire range of Federal efforts allocated to human exposure measurements. However, EPA devoted about \$6.7 million to such efforts in 1993, and the U.S. Department of Agriculture (USDA) allocated about \$11 million for analyzing pesticide residues on produce.

As would be expected for activities as broad as risk assessment research, some fields of inquiry have received more funds, some fewer. However,

Figure 4-4-Federal Research Related to Chemical Toxicology, 1980-92
(In millions of dollars and full-time equivalents)



Chapter 4: Setting Priorities for Risk Assessment Research 97



Dollars
FTE

m Basic Testing Method
Basic Testing Method

SOURCE: Office of Technology Assessment, 1993, based on data from Review of Current DHHS, DOE and EPA Research Related to Toxicology, Fiscal Years 1982 through 1991, National Toxicology Program, U.S. Department of Health and Human Services.

Table 4-2A—Health Risk Research and Development Estimates, 1993
(In millions of dollars)

Agency	Health risk research*		Agency total: health or biomedical research**
	Total	Methods	
National institute of Environmental Health Sciences.	129.0	14.0	251.2
Department of Energy	10.0 ^e	3.0 ^e	90.0 ^e
Department of Defense	19.6	2.5 ^b	300.0 ^f
U.S. Department of Agriculture	11.5 ^d	0.5 ^d	11.5 ^a
Agency for Toxic Substances and Disease Registry	16.9	0.0	16.9 nd
Environmental Protection Agency.	32.0	21.30	49.0 ^f
Food and Drug Administration (other than NCTR).	13.0a	3.5 ^a	13.0 nd
National Center for Toxicological Research	33.6	7.6	38.92 ^a
National institute for Occupational Safety and Health.	49.0	6.1	49.0 ^f
National Cancer institute.	82.0 ^e	4.4a	1,981.4
Other NIH	140.0 ^e	2.2 ^e	6,929.9
Alcohol, Drug Abuse, and Mental Health Administration.	64.0 ^e	0.0 ^e	1,164.1
Total	600.6	65.1	10,894.5

a Estimate based on agency's 1992 funding for research on toxicology, as reported in the National Toxicology Program Review of current DHHS, DOE, and EPA Research Related to Toxicology, Fiscal Year, 1992.

b Calculated as 13 percent of agency R&D for health.

c Steinberg, 1993, *Journal of NIH Research* 5:35, Data on biomedical research, which excludes \$210 million for breast cancer research.

d Data supplied by the U.S. Department of Agriculture, budgeted under expenses and not research and development.

e Research to improve Health Risk Assessment program estimated to be \$5 million; \$21.3 million is sum of funding for human exposure, health effects, and risk assessment methods.

f Figure represents Health Effects Research Laboratory total budget; EPA-wide data are not available.

nd No data (research related to toxicology was used).

● Based on data from the OTA survey of agency resources.

● *U.S. Congress, CRS, 1993. Research and development funding: fiscal year 1993; issue brief (IB2062).

SOURCE: Office of Technology Assessment, 1993.

environmental health research funding has neither kept up with the increase in health research nor increases in environmental mandates that depend on that research for decisionmaking. Methodological research, in particular, seems inadequately supported, despite the most immediate promise that OTA sees for this research to improve risk assessment.

NATIONAL RESEARCH PRIORITIES

A complex interplay among social, economic, and scientific factors influences national research priorities. Depending on the political and social milieu of the Nation, Government research to protect the health of the public from environmental agents fluctuates between being more applied or more basic in nature. In response to the environmental and social activism of the 1960s and 1970s, policymakers called for the Government to play a larger role in applying the advances

of research and development to achieving societal goals, including environmental protection and improved public health (Smith, 1990). In contrast, the Reagan Administration during the 1980s channeled research resources toward national security and basic science (Smith, 1990). Judging from the early budget figures, science policy in the Clinton Administration will return to emphasizing applied research and development (Long, 1993).

Mission-oriented research, a type of applied research, is directed toward identifiable ends related to meeting an agency's responsibilities. After World War II, mission-oriented research became established in agencies, and basic research tended to be located in universities (Smith, 1990; U.S. Congress, OTA, 1991). The role of the Federal Government in support of research grew as regulatory decisions became increasingly technical and complex, and more science-based expertise was needed for agency decisionmaking.

Table 4-2 B-Research Related to Toxicology, 1992
(In millions of dollars)

Agency	Chemical Toxicology*		Agency total: health or biomedical research**
	Total	Methods	
National Institute of Environmental Health Sciences.	154.6	22.0	251.6
Department of Energy	9.8	2.7	90.09
Department of Defense	15.0 ^b	2.8	300.0 ^d
U.S. Department of Agriculture	11.8 ^e	0.5 ^f	11.8 ^g
Agency for Toxic Substances and Disease Registry	17.5	0.0	17.5~
Environmental Protection Agency.	47.3	35.4	47.3 nd
Food and Drug Administration (other than NCTR).	12.5	3.5	12.5 nd
National Center for Toxicological Research	30.9	16.2	30.0 [@]
National Institute for Occupational Safety and Health.	4.4	2.7	4.4 nd
National Cancer Institute.	82.0	4.4	1,947.6
Other NIH	139.7	2.2	6,729.8
Alcohol, Drug Abuse, and Mental Health Administration	64.0	0.0	1,131.4
Total	589.5	91.6	10,574.8

a Estimate is based on personal communication.

b The Army portion is estimated using 1993 data from Department of Defense.

c Calculated as 13 percent of agency research and development for health, based on earlier allocations.

d Steinberg, 1993, *Journal of NIH Research* 5:35, Data on biomedical research, which excludes \$25 million for breast cancer research.

e Data supplied by U.S. Department of Agriculture, budgeted under expenses and not research and development.

f N. data available. Health risk R&D used. USDA FY 1991 health R&D \$115 million, from NIH databook.

nd No data (research related to toxicology was used).

● Review of current DHHS, DOE, and EPA Research Related to Toxicology, Fiscal Year 1992, National Toxicology Program, U.S. Department of Health and Human Services.

● *U.S. Congress, CRS, 1993. Research and development funding: fiscal year 1993; issue brief (IB2062).

SOURCE: Office of Technology Assessment, 1993.

Under congressional direction, agencies pursued research to support a “scientific base for public policy,” with EPA emerging as “the epitome of the new expert agency” (Jasanoff, 1990).

Many of the researchers surveyed by OTA claim that Federal funding, divided between applied and basic research, allows risk assessment research “to slip through the cracks.” Consequently, most research efforts to improve risk assessment have inadequate support. No study section at the National Institutes of Health, for example, reviews proposals for health risk assessment research. At a more general level, few funding opportunities exist for multidisciplinary collaborations among basic and applied scientists, despite the acknowledged need for such endeavors to make risk assessment research more effective (U.S. DHHS, 1991c).

Below the surface of the debate over the balance between basic and applied research lie questions about the objective and nature of the

research on risk assessment that the Government should be supporting and conducting. The environmental movement of the 1960s, for example, stimulated intense Federal efforts to identify pollutants that can affect human health and the environment. As a result, NTP was established to set national priorities for toxicity testing (U.S. DHHS, 1991a), and both supporters and critics of the program consider it the Nation’s premier testing program (Moolenaar, 1992; Ringen, 1992).

If tests of a commercially important substance reveal that hazards exist, manufacturers or users who want to retain the commercial uses for the substance may perform additional research to clarify the nature of the hazard and support quantitative risk assessment. In efforts to shift research priorities, some scientists and industry spokespersons have called for the Government to conduct more research on the mechanisms of toxicity (Abelson, 1993; Gori, 1992; Moolenaar, 1992). Such a controversy currently surrounds the

proposed directing of NTP research away from toxicity testing and rodent bioassays and toward studies on such mechanisms (U.S. DHHS, 1992). As the debate is framed, toxicity tests, on the one hand, can identify potential hazards to public health, which can trigger intervention strategies designed to prevent exposures to the agent. On the other hand, mechanistic studies can determine the applicability of the results of toxicity tests to predict human risks from exposure.

The debate suggests that these types of research—toxicity testing and mechanistic research—have necessarily mutually exclusive objectives, that resources can be used for either type of research but not both. In fact, the NTP Board of Scientific Counselors concluded that these research activities can be integrated to complement each other (U.S. DHHS, NTP, 1992). The results of toxicity studies often illuminate fruitful avenues of mechanistic research. Similarly, data from mechanistic studies can illuminate the implications for human health risk of the results from toxicity testing. In addition, mechanistic research provides a foundation for identifying untested chemicals and chemical classes for toxicity testing.

The debate over the role of Government research does not end at NTP. Related discussions are heard concerning the research priorities of NTEHS, NCTR, and EPA.

Setting National Priorities

In the past, the United States has embarked on national multiagency efforts in public health. Some were strikingly successful; others were not. As part of a worldwide campaign, this country aggressively attacked the childhood scourges smallpox and polio, culminating in the complete eradication of smallpox and the virtual eradication of polio. The U.S. ‘wars’ on cancer in the 1970s (Epstein, 1979) and AIDS in the 1980s (Joseph, 1992), however, produced less tangible results, but those consequences may be more a reflection of the complexities of those diseases

than of the Federal effort. Generally, the scientific process is difficult to reconcile with a war mentality. Science proceeds in discreet, incremental, and often publicly imperceptible steps confounded by missteps and mistaken paths (Kuhn, 1962). Moreover, the most brilliant technological breakthroughs often are not planned; recombinant DNA techniques revolutionized cancer biology, but they were not anticipated in the detailed planning that went into the war on cancer. Still, although cancer and AIDS are problems that currently lack solutions, indisputable progress has been made in both cases. Indeed, the recent advances in the molecular biology of cancer, for example, offer promise and optimism unimagined in the ‘war years’ (Barrett, 1993).

Arguably, the President has the most influence in setting national priorities for research at the agencies. With a variety of administrative tools, such as executive orders (Olson, 1984), the President can emphasize or deemphasize certain areas of scientific research. The increased research on cancer in the 1970s, for example, stemmed from presidential efforts (Epstein, 1979; Rushefsky, 1986).

Related to presidential influence, the degree of centralized authority at the national level has implications for implementing a national research effort. A centralized program, often a multiagency activity coordinated through a central authority such as the Executive Office of the President, provides focus and direction, but the agencies lose a portion of their authority. A decentralized effort, in contrast, gives the agencies more autonomy but the objectives can be less defined, the effort more fragmented, and the goals of the agencies given more importance than goals of the effort.

In centralizing research efforts, the President has at his command several administrative processes to set national priorities. The Federal Coordinating Council on Science, Engineering, and Technology (FCCSET), which the Bush Administration greatly strengthened, serves as the Federal Government’s focal point for setting

priorities within the executive branch. Overseen by the White House Office of Science and Technology Policy, FCCSET policymakers and scientists from various research agencies operate in specialized subcommittees and working groups, directed at specific problems. Under D. Allan Bromley, President Bush's science adviser, FCCSET conducted "crosscuts," in which an interagency committee inventors Federal activities and establishes objectives and priorities for coordinating basic and applied research in high-impact areas. Some examples include research on global change, high-performance computing and communications, mathematics and science education, advanced materials and processing, and biotechnology (Bromley, 1992).

FCCSET in 1991 and 1992 had some focus on health risk assessment research: its Subcommittee on Risk Assessment of the Committee on Life Sciences began an effort to identify future health risk assessment research needs. Although this activity was not aimed at coordinating research projects, the activities of the subcommittee were a first step in creating an inventory of ongoing research, which could be useful in future coordinating efforts. A research inventory would have allowed FCCSET members to identify redundant research, areas of little or no activity, and research efforts that could be usefully integrated across agencies. However, this project apparently has been put quietly to rest with the transition to the Clinton Administration. OTA carried out a similar survey as part of this assessment (see ch. 3).

According to the National Performance Review, the Clinton Administration is planning to eliminate FCCSET. In its place, the White House will coordinate agency research programs through a new National Science and Technology Council. This new council combines FCCSET with the National Materials Council and the National Space Council, but it will remain within the Office of Science and Technology Policy (Hanson et al., 1993).

The Office of Management and Budget (OMB) also influences executive branch decisions con-

cerning science priorities. Through its review function, OMB can delay research and regulatory activity (Olson, 1984). For example, OMB currently reviews proposed Federal research involving human subjects. In many cases, the resulting delay effectively diminished or even halted research in certain areas, such as in the use of questionnaires in epidemiologic research (Lilienfeld, 1993).

The legislative branch also sets and influences national research priorities. Congressional members and committees charged with responsibility for broad areas, such as environmental protection or public health, may influence the direction of research in those areas through legislation, appropriations, or reports. Similarly, congressional research agencies such as the General Accounting Office or OTA can affect national priorities through their analyses of related issues. For example, congressional representatives (Brown, 1993) and congressional reports (e.g., U.S. Congress, OTA, 1991; U.S. Congress, House Committee on Science, Space, and Technology, 1992) recently suggested changes in U.S. research policy that would link research more tangibly to national goals.

When a particular topic is designated a national research priority, it is accorded leadership at the highest echelons of government, strategic initiatives that span many Federal agencies, and resources that are commensurate with the magnitude of the problem. Health risk assessment research possesses none of those hallmarks. Moreover, OTA did not find a systematic, national multiagency process for setting research priorities for improving health risk assessments. Apparently, the FCCSET subcommittee on risk assessment research needs will not release the results of its survey of Federal research efforts. As a result, that effort has had little impact, if any, on the direction of research. Some observers and participants remain sanguine about the FCCSET process, but the predictions that the research needs study will end without a product are strong counter arguments. The proposed

National Science and Technology Council is designed to have more “teeth” than FCCSET (Hansen et al., 1993).

In examining agency research, OTA found that Federal research on health risk assessment, as a whole, is largely decentralized. Agencies have different priorities because they have different legislative mandates and missions. Within agencies and departments, risk assessment research programs conduct research in support of their parent organizations. This behavior parallels that seen for environmental research and development (Schaefer, 1991; Carnegie Commission, 1992) and for the Federal research and development effort in general (U.S. Congress, OTA, 1991). Leadership from the White House or Congress could improve health risk assessment research by bringing cohesion and focus to research goals.

As pointed out in chapter 2, more than 50 assumptions have been identified that are used in risk assessments. Use of those untested assumptions underlines the promise of research to illuminate some of the areas of current ignorance. A coordinated effort, for example, could determine the extent to which research can reduce the dependence on assumptions. More than a decade has passed since the NRC report, and research efforts have expanded on some of these, but priority-setting to increase the impact of research does not exist. Assumptions that can be replaced by research need to be distinguished from assumptions that cannot be replaced by research.

AGENCY PRIORITIES

An agency’s risk assessment research depends on priorities in its mission, its enabling legislation

(table 4-3), and court decisions. In line with their missions, the agencies that conduct research related to risk assessment can be separated into those with responsibilities for risk management (regulatory agencies) and those without such responsibilities (research agencies). Risk management, as described in chapter 5, integrates and synthesizes myriad information (such as economic, political, and technological factors) along with risk assessments, to set, implement, and enforce regulatory standards (NRC, 1983).

Research at the regulatory agencies, especially at EPA, the Occupational Safety and Health Administration (OSHA), Consumer Product Safety Commission (CPSC), and FDA, is mostly driven by regulatory needs, as mandated by congress. Regulatory agencies need chemical-specific data to set standards and establish priorities for rule-making (Rosenthal et al., 1992). EPA’s authority to conduct environmental health research derives mainly from the major Federal laws protecting public health and the environment. The research programs of its Health Effects Research Laboratory (HERL) are mandated in at least six major pieces of legislation, and funding is appropriated on a medium-specific basis.⁵ By requiring EPA to protect public health, the statutes give the agency discretionary authority to conduct research on health effects.⁶

Although the Occupational Safety and Health Administration (OSHA) is not required under the Occupational Safety and Health Act (OSH Act) to conduct risk assessments, a U.S. Supreme Court decision on workplace exposure to benzene requires OSHA to determine whether risks are “significant” before imposing regulation.⁷ Risk

⁵The research programs are mandated under one of the following: Clean Air Act; Safe Drinking Water Act; Federal Insecticide, Fungicide, and Rodenticide Act; Toxic Substances Control Act; Comprehensive Environmental Response, Compensating and Liability Act; or Resource Conservation and Recovery Act (U.S. Congress, CRS, 1993).

⁶The Environmental Research and Development Demonstration Act (ERDDA) of 1976 brought EPA’s research programs under a single mandate, but authorization for it ended in 1981 (U.S. Congress, CRS, 1993). Recently, the Subcommittee on Technology, Environment, and Aviation of the House Science, Space, and Technology Committee has been developing the Environmental Research, Development and Demonstration Act of 1993 (H.R. 1994).

⁷OSHA does not perform risk assessment research (Martonik, 1992). The National Institute for Occupational Safety and Health, the research arm of OSHA, conducts studies on workplace agents that affect worker safety and health (Mintz, 1984).

assessment is the method OSHA uses in making that determination (Mintz, 1984).⁸The OSHA Act stipulates that the National Institute for Occupational Safety and Health (NIOSH) would conduct health effects research for OSHA rulemaking (P.L. 91-596).

Among the Federal agencies, DHHS has the broadest set of research responsibilities for investigating possible health risks. Within DHHS, are the research agencies of the Public Health Service—specifically, NIEHS, NCI, NCTR, NIOSH, and the Agency for Toxic Substances and Disease Registry (ATSDR) (see app. B). The charters of these agencies mandate a research mission.

The Departments of Defense (DOD) and Energy (DOE) are neither regulatory agencies nor public health research agencies. However, they perform and support research on health risks as part of their risk management responsibilities (Macys, 1993; U.S. DOE, 1991).

To gain insight into agency research priorities, OTA examined the funding and FTEs as a percentage of the total contribution to research in toxicology by NIEHS, NCI, NCTR, EPA, and CFSAN, as reported in the NTP review.⁹This additional analysis attempts to get a snapshot of the trends in resource allocation to the three areas of toxicological research—methodological, basic, and chemical-specific data development, by the agencies most active in this research. As shown in figure 4-5A, the agency resources are presented as percentages of the total for the years 1982, 1986, and 1991. For these agencies in those years, funding for basic research increased from 41 to 53 percent, toxicology testing declined from 45 to 24 percent, and methodologic research increased from 14 to 22 percent. Figure 4-5B provides a snapshot for the intramural researchers at the agencies and the nature of their research. In 1991,

39 percent of the full-time equivalents (FTEs) were conducting basic research, 24 percent in testing, and 34 percent in methods research. The relative proportions of FTEs to funding in dollars suggests that most basic toxicological research is supported by extramural grants, whereas most methodological research is conducted in intramural research.

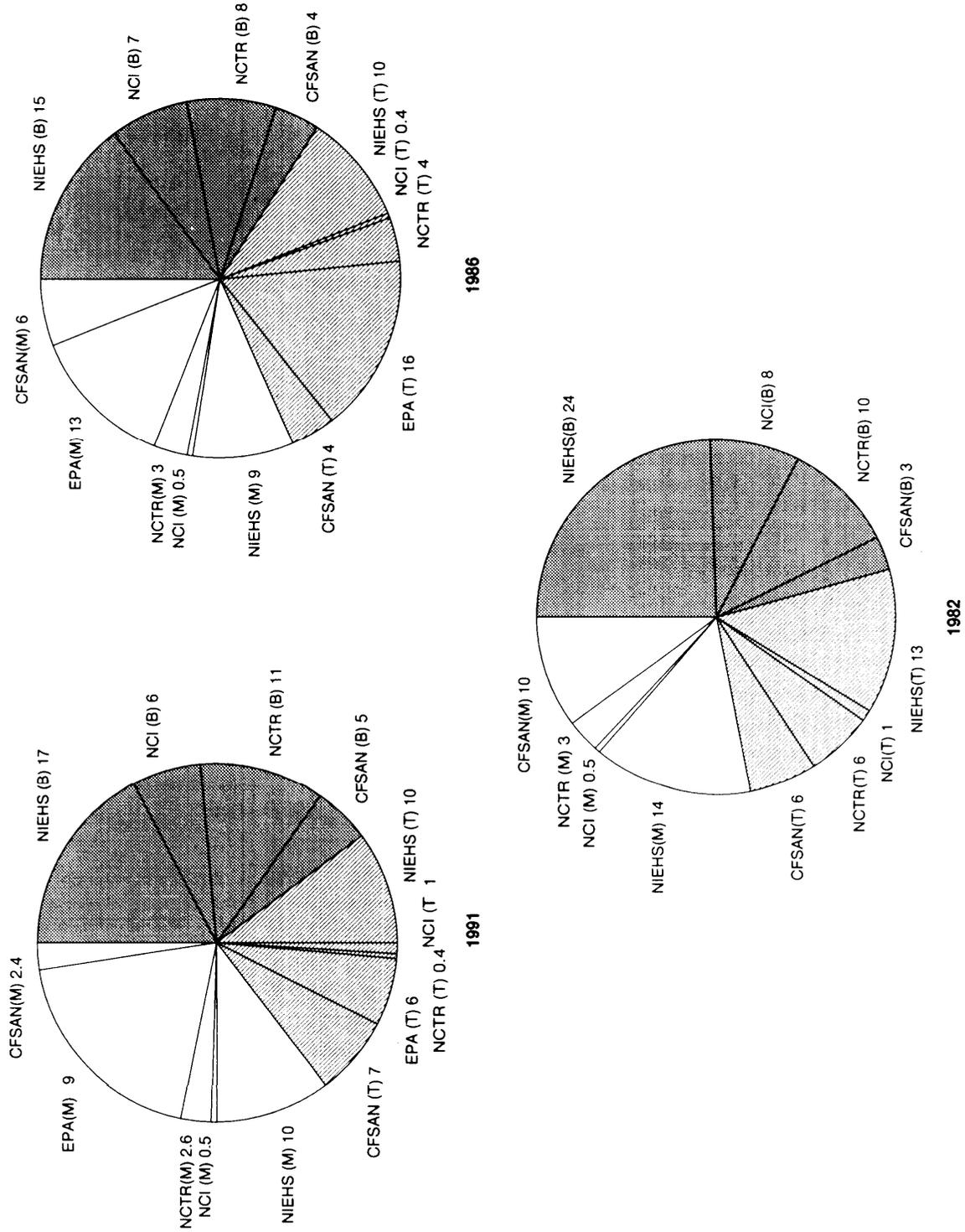
OTA estimates that in 1993 the agencies will spend nearly \$600 million on health risk research, but that only \$65 million of that total will be spent on methodological research. Even considering that these estimates are based on agency definitions of research, methodological research receives disproportionately less than the other areas of research. In times of restricted resources and in the wake of congressional imperatives, the agencies tend to maintain their existing core programs. Thus, regulatory agencies focus on chemical-specific data development, and research agencies perform basic research. Methodological research remains marginalized in the process.

A variety of reasons can be forwarded to explain the relative neglect of methods research. Incorporating the results of research into policy requires overcoming substantial bureaucratic hurdles and usually necessitates some sort of scientific consensus on an issue. (Chapter 5 discusses the difficulties in changing agency policy.) Furthermore, agencies—especially regulatory agencies, which are bureaucratic by nature and slow in responding to changes—must gain the acceptance of the scientific community before they adopt new methodologies (Jasanoff, 1990; Rosenthal et al., 1992). That sort of support is crucial to providing credibility to new policies. Moreover, methodological research requires validation with experimental data, an activity to which agencies allocate few resources. These obstacles to the use

⁸The 1981 U.S. Supreme Court decision on OSHA's workplace standard for benzene states that rulemaking must protect workers from 'significant' risk. Significance under the Occupational Safety and Health Act has since been interpreted by OSHA to be one adverse effect, such as cancer, in 1,000 workers (Mintz, 1984; Rodericks et al., 1987).

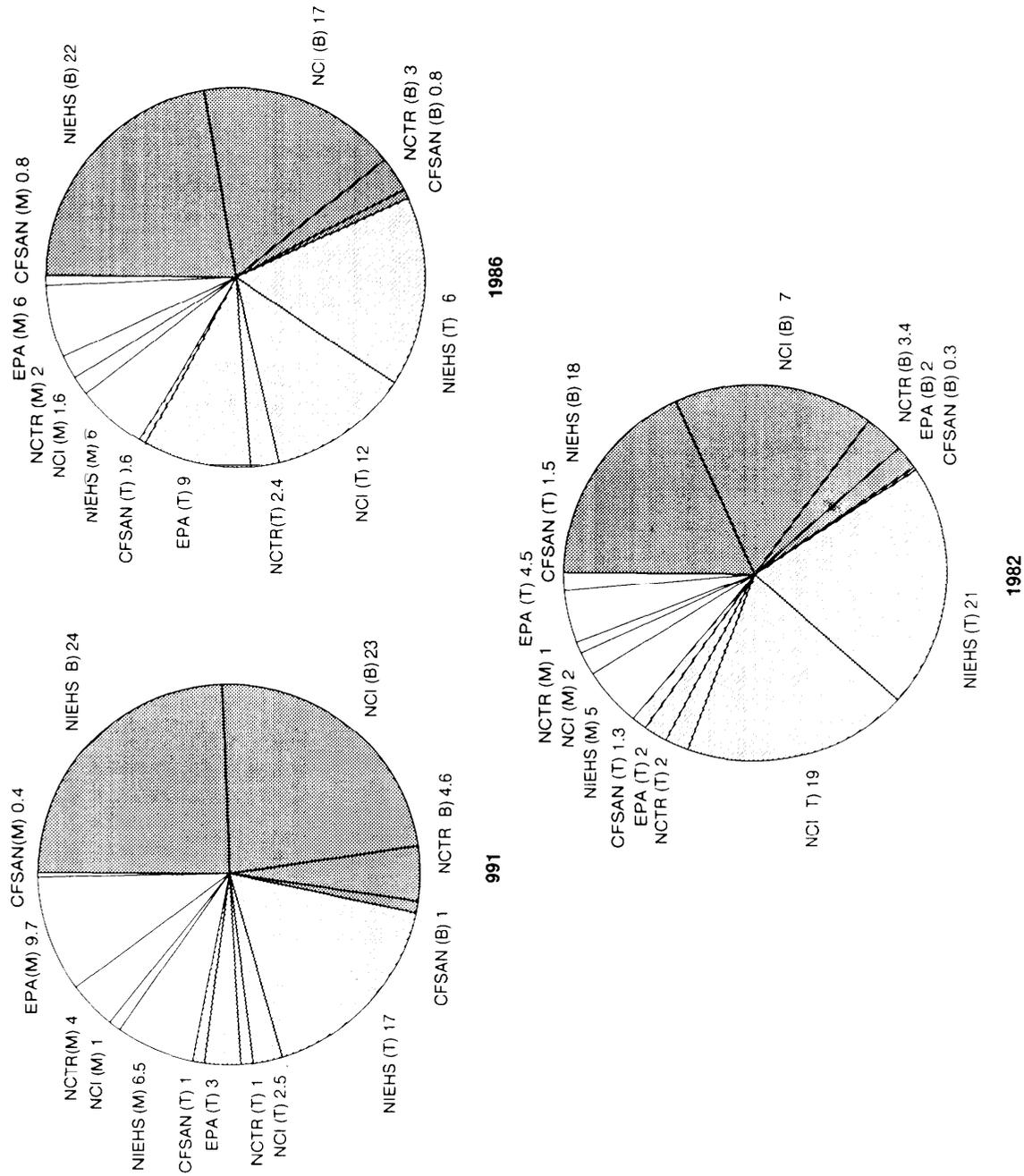
⁹OTA did not include the resources of NIOSH in this analysis because their support reported to NTP are resources committed to the NTP program and is not representative of the total NIOSH contribution to this research.

Figure 4-5A—Agency Shares of Health Risk Research by Research Area, 1982, 1986, and 1991 (Funding in Dollars)



SOURCE: Office of Technology Assessment, 1993, based on data from Review of Current DHHS, DOE, and EPA Research Related to Toxicology, Fiscal Years 1982, 1986, and 1991. National Toxicology Program, U.S. Department of Health and Human Services.

Figure 4-5B—Agency Shares of Health Risk Research by Research Area, 1982, 1986, and 1991 (Personnel in Full-Time Equivalent)



SOURCE: Office of Technology Assessment, 1993, based on data from Review of Current DHHS, DOE, and EPA Research Related to Toxicology, Fiscal Years 1982, 1986, and 1991. National Toxicology Program, U.S. Department of Health and Human Services.

Table 4-8 Key Features of Federal Laws Regulating Toxic Substances

Statute	Regulatory authority (regulatory agency)	Toxic substance or effect of concern
Part I--Licensing Laws		
Federal Food, Drug, and Cosmetic Act	Control levels of added substances (FDA)	“Any poisonous or deleterious substance which may render it injurious to health”
	Control levels of natural components of food (FDA)	“Poisonous or deleterious . . . does not ordinarily render it injurious to health”
	Control levels of environmental contaminants (FDA)	“Poisonous or deleterious . . . does not ordinarily render it injurious to health”
	Set (EPA) and enforce (FDA, USDA) tolerances for pesticide residues on food and feed crops	“Poisonous or deleterious. . . not general recognized as safe for use . . . to the extent necessary to protect the public health”
	Regulate introduction of new drugs and biologics (FDA)	“Substantial evidence at safe and effective:” no “imminent hazard to public health”
	Report on adverse reactions to drugs (FDA)	“Any adverse experience . . . includes any side effect, injury, toxicity, or sensitivity reaction”
	Label cosmetics (FDA)	“Poisonous or deleterious . . . may render it injurious”
Federal Insecticide, Fungicide, and Rodenticide Act	Register pesticides (EPA)	Will not generally cause any unreasonable risk to man or the environment”
Toxic Substances Control Act	Require testing of existing chemicals where data are inadequate to assess risk (sec. 4); prohibit introduction into commerce of chemicals that will present an unreasonable risk (sec. 5); restrict or prevent production, use, or disposal of existing chemicals that present unreasonable risk (sec. 6) (EPA)	Unreasonable risk of injury to human health or the environment. . . includ[ing] carcinogenesis, mutagenesis, teratogenesis, behavioral disorders, cumulative or synergistic effects, and any other effect . . .
Part I--standard-setting Laws		
Clean Air Act	Conduct research on air pollution (EPA)	“Adverse effects on health, including, but not limited to, behavioral, physiological, toxicological, and biochemical effects”
	Set air quality standards; regulate emissions of hazardous air pollutants; set standards for vehicle emissions, fuels, and fuel additives (EPA)	“Endanger public health”

Federal Water Pollution Control Act; Clean Water Act	Set effluent standards for water; establish water quality criteria (EPA)	"Identifiable effects on health and welfare"
Safe Drinking Water Act	Set MCLs and MCLGs for public drinking water supplies (EPA)	"May have an adverse effect on the health of persons"
Consumer Product Safety Act	Promulgate consumer product safety standards (CPSC)	"An unreasonable risk of injury"
Federal Hazardous Substances Act	Ban hazardous substances for household use (CPSC)	"Toxic . . . may cause substantial personal injury or substantial illness"
Federal Mine Safety and Health Act	Set standards for airborne contaminants in mines (MSHA)	"Protection of life and prevention of injuries. . . material impairment of health or functional capacity"
Occupational Safety and Health Act	Set standards for airborne contaminants in the workplace (OSHA)	"Material impairment of health or functional capacity"
Part 111-Control-Oriented Laws		
Comprehensive Environmental Response, Compensation, and Liability Act; Superfund Amendments and Reauthorization Act	Fund cleanup of hazardous waste sites; designate reportable quantities for environmental release; report on community preparedness and release; prepare toxicity profiles on contaminants (EPA)	"Substantial danger to the public health or welfare"
Controlled Substances Act	Control drugs that have potential for abuse (USDJ, FDA)	"Substantial and detrimental effect"
Lead-Based Paint Poisoning Prevention Act	Determine, if possible, a safe level of lead in paint (CPSC)	Poisoning of children by lead-based paint
Marine Protection, Research, and Sanctuaries Act	Regulate ocean dumping (EPA)	"Adversely affect human health, welfare or amenities"
Poison Prevention Packaging Act	Promulgate standards for packaging substances that could produce effects of concern (CPSC)	"Serious personal injury or serious illness"
Resource Conservation and Recovery Act	Regulate the handling of hazardous wastes; list hazardous wastes on basis of constituents (EPA)	"Protect human health . . . serious irreversible or incapacitating reversible illness . . . substantial present or potential hazard"

NOTES: FDA - Food and Drug Administration; EPA. Environmental Protection Agency; USDA. U.S. Department of Agriculture; USDJ. U.S. Department of Justice; CPSC. Consumer Product Safety Commission; MSHA - Mine Safety and Health Administration; OSHA - Occupational Safety and Health Administration; MCL - maximum contaminant level; MCLG - maximum contaminant level goal.

SOURCE: Office of Technology Assessment, 1993.

of the results raises important questions about the usefulness of methodological research and its likely impact on policy.

Bureaucratic reluctance to accept new methods provides an especially strong disincentive for researchers. Why do the work if it is likely to be ignored. Individual promotions and advancement in the scientific community are predicated on research output and visibility. As a result, researchers either conduct chemical-specific research, which responds directly to agency needs, or basic research, which is held in higher esteem in the scientific community and is likely to be published in more prestigious scientific journals. Taken all together, there are few incentives for a researcher to conduct methodological research: the agencies consider it a secondary priority and allocate fewer resources to it, and the results of the work face substantial hurdles before being incorporated into agency practice or being accepted by the scientific community.

In addition to the mission of an agency and its enabling legislation, each agency has its own “culture” as well, which is a powerful determinant of future research directions (Yosie, 1987; Zimmerman, 1990). The collective knowledge of agency personnel often governs the “way things are done,” reflecting the style of the agency’s management (U.S. Congress, OTA, 1991; Wilson, 1989). Moreover, the composition and professional interests of an agency’s work force can influence research priorities. NIEHS affords an example of the role agency culture can play in establishing the direction of research. Because scientists at that institute consider themselves basic scientists, some of them have a certain disdain for the more applied research needed for regulatory decisionmaking (Stone, 1993). Consequently, those scientists rebelled in 1992 during the agency’s reorganizing and reordering of its priorities, which required it to conduct more applied research; the tension from that confrontation resulted in some scientists leaving NIEHS. Over the long term, the effects of NIEHS’s new structure and direction remain to be seen.

PROGRAMMATIC PRIORITIES AND PROGRAM MANAGEMENT

An agency usually divides its research into programs or divisions of researchers who share a common discipline or objectives. For risk assessment research, the disciplinary distinctions are often found in the disciplines of the environmental health sciences—for example, EPA’s HURL has programs in, among other areas, neurotoxicology, immunotoxicology, genetic toxicology, and reproductive and developmental toxicology. Rarely, do Federal programs cut across disciplines; the exceptions include EPA’s Research to Improve Health Risk Assessment program and NTEHS’s Laboratory of Biochemical Risk Analysis.

Setting priorities at the program level is generally a more developed—that is, both a more systematic and more formal—process than at the agency or national levels. Generally, one of two distinct types of management methods is used to determine program priorities for individual research projects (U.S. Congress, OTA, 1991). One style, termed “bottom-up,” allows research ideas and priorities to originate with individual researchers, who communicate those ideas to their superiors or to grant managers. As ideas rise through intermediate levels of management to the upper tier of program decisionmakers, the better and more important proposals are selected. In contrast, “top-down” management has the most senior decisionmakers in an agency deciding the priorities for research. Those directives are transmitted down the organizational ladder in consultation with managers, eventually reaching researchers.

OTA observed both styles of management in its survey of risk assessment research, as well as a mixture of styles, which is consistent with federally funded science in general (U.S. Congress, OTA, 1991). At DOD, managers at all levels exert a great deal of influence in selecting and funding projects. But research agencies such as NIEHS and NCI employ mostly bottom-up management,

with individual researchers initiating projects and influencing the directions of research. The styles of EPA and DOE are a mixture of the two: priority-setting is responsive to the choices of top management but also provides an opportunity for initiative by individual investigators. The management style of an agency mirrors its research needs and whether it has risk management responsibilities. Agencies that use the results of research for decisionmaking require data for their short-term regulatory needs and rely on top-down approaches to engender those data. In contrast, agencies seeking to expand the scientific knowledge base support investigator-initiated projects.

ADMINISTRATIVE TOOLS FOR PRIORITY-SETTING

Changes in leadership often alters an agency's objectives and organization. New directors took over the reins of NIEHS in 1991, and EPA and National Institutes of Health (NIH) in 1993, and FDA is completing its search for a new director of NCTR. Those new leaders are restructuring or will restructure their agencies along the lines laid down by the larger Government organization to which they are responsible. A past example of such leadership is the former director of the NIH, who initiated strategic planning for the institutes (Healy, 1992). All of the institutes within NIH, including NIEHS, were developing strategic plans for future priorities, but the future of this initiative is now very much in doubt. What is clear is that initiatives launched and policies set by a new director of NIH will influence NIEHS'S future.

Restructuring occurs under new directors and under established directors when conditions, needs, or wants dictate. At the agency level, NIEHS's new director has restructured programs following consultation with advisory panels (Olden, 1992). A new FDA commissioner restructured the Center for Food Safety and Nutrition and gave NCTR

the mandate to integrate its research activity more closely with FDA's regulatory needs.

Yet even though agency directors can influence, shape, and promote research priorities, they must solicit scientific, technical, and stakeholder opinions to satisfy procedural rules and maintain credibility, not only within the agency but also the scientific community and other agencies in the Federal Government. Agencies have a variety of common administrative tools for establishing the directions their research will take.

Use of Advisory Committees

To change directions or to set new policy, agency directors often employ outside experts to evaluate research programs and recommend policy shifts (Smith, 1992; Zimmerman, 1990). Internally, the agencies also receive advice from institutional committees established as science advisers. Expert committees, which can be set on a continuing or ad hoc basis, provide scientific credibility for administrative decisions (Jasanoff, 1990; Smith, 1992). Carrying out the recommendations of these external and internal advisory panels remains more problematic.

EPA uses a variety of established and ad hoc advisory committees to assist it in setting priorities for research. The role of EPA's Science Advisory Board has expanded from that of an independent technical reviewer of EPA documents to include advising on science policy (Jasanoff, 1990; Yosie, 1991; Smith, 1992). When it was formed in the early 1970s, the board was meant to function as an external review body located in the Office of Research and Development. In 1976, however, it was relocated (and organizationally "elevated") to the Office of the Administrator (Yosie, 1991).¹⁰

EPA committees have released documents recently that have proved influential in agency actions. Among the 10 committees of the Science Advisory Board (SAB), the Research Strategies

¹⁰ The 1978 Environmental Research and Development, Demonstration Act codified the board's mission and mandated that the Science Advisory Board report directly to the administrator (42 U.S.C. 4365 (a)(c)(e)).

Advisory Committee examines scientific issues and problems that cut across the agency's many offices and sets research priorities (Barnes, 1992). In 1988 and 1990, the Committee released two influential documents, both of which concluded that EPA should set priorities for its research and regulatory programs based on magnitudes of risk (U.S. EPA, SAB, 1988, 1990). (On a much more defined level, the EPA SAB provides advice about such discrete problems as indoor and waterborne radon; see chapter 6.) In addition to SAB, EPA forms expert panels for specific purposes, such as the ad hoc 'blue-ribbon' panel of outside experts that is evaluating EPA's science base. The panel's report concluded that the agency's science programs should be given greater visibility and access to agency administrators (U.S. EPA, 1992).

NIEHS also employs outside experts in environmental health on its Boards of Scientific Counselors to evaluate priorities and research directions. Three such boards and several subboards retrospectively reviews the science of the institute and other agency matters (Olden, 1992; Griesemer, 1992; Schwetz, 1992; Tennant, 1992). For example, the institute based its recent restructuring on extensive meetings with those permanent and ad hoc advisory councils and boards. In an attempt to be responsive to the public as well as the scientific community, NIEHS administrators are also holding meetings with public organizations across the country and are pursuing discussions with congressional representatives (Olden, 1993).

To understand the relative importance of a particular field of study, NIEHS convenes various consensus conferences and workshops. The 1991 House Appropriations Bill directed the advisory council for NIEHS to identify those environmental problems threatening public health over the coming decade. In response to the congressional mandate, the council formed the Fourth

Task Force for Research Planning in the Environmental Health Sciences (U.S. DHHS, 1991c). The task force identified and characterized the areas of particular challenge and promise in the environmental health sciences and influenced the "big-picture" directions of the agency (Olden, 1992; U.S. DHHS, 1991c).

Outside experts are important to the workings of other agencies as well. In addition to the regular meetings of NCI's directors and associate directors, the agency uses the recommendations of the National Cancer Advisory Board to help set priorities. (The board's membership includes representatives from EPA, NIEHS, NCI, OSHA, and other agencies.) Moreover, an external advisory board triggered the reorganization at NCTR. The Edwards Commission report on FDA provided the background for reconciling investigator-initiated research at NCTR with the regulatory needs of FDA (U.S. DHHS, 1991 b). The agency redesigned its Science Policy Committee in 1992 to address the scientific issues arising from its new priorities (Anson, 1993).

Funding Mechanisms

Agencies have a number of mechanisms by which to fund research projects. Resources can be allocated through intramural or extramural grants, cooperative agreements, contracts, and in-house work (Jasanoff, 1990; U.S. Congress, OTA, 1991).

Grants and contracts are largely used to fund extramural research done at locations other than Federal facilities. Agencies often use a two-tiered process in determining which grant applications will be funded. They select applications for funding based on the scientific and technical 'merits' of the work, as determined by peer review.¹¹ The product of a peer review of grant proposals is a priority score, by which that proposal can be ranked with others. By design, peer review is supposed to be a self-regulatory

¹¹ Peer review is a process by which scientists involved in an area of research judge the scientific merit, technical competence, and significance of proposals by their professional peers. In general, peer-review is conducted by better known and more successful scientists.

process for scientists that obviates the need for external controls (Jasanoff, 1990). Although peer review possesses a variety of positive attributes that undoubtedly contributes to this country's scientific and technological successes, nonetheless, the process has several faults, such as inconsistency and the inability to guarantee quality in science (Jasanoff, 1990; US Congress, OTA, 1991).

Determination of mission relevance is the second tier of review. It can justify shifting resources to particular areas of research that may not earn the highest marks in peer review. Such alterations are unusual, even rare, in basic research. They do occur, however. NIEHS, for example, may redirect funds to projects that receive less favorable priority scores if the areas of research need further development or appear particularly promising (Olden, 1992). Ultimately, grant-sponsoring agencies are accountable to Congress; thus, both scientific and political factors are incorporated into decisions on grants.

Agencies also use contracts to support work of a specific, technical nature. Contract proposals do not undergo the type of peer review used for grants applications. Even though many contract proposals go through a competitive bid and selection process, the process can lend itself to abuse. For example, EPA has been criticized for its extensive use and mismanagement of the contracts process (U.S. Congress, GAO, 1992).

Extramural funding by an agency—for example, to individual university investigators—represents an effort to provide national leadership in a field of study. Extramural grants are used to support university research and as seed money to develop fields of research. In reality, some fields of research are almost completely dependent on Federal support. Generally, basic research, which can have long-term payoffs, is seen as especially deserving of Federal support. Many investigators interviewed by OTA commented that extramural funding for risk assessment research is inadequate because the research is considered too applied to be supported by basic research

funds and too basic for applied research funds. Extramural funding for risk assessment research also tends to be unstable, which may result in researchers being forced to leave the field and new researchers being dissuaded from entering because of the limited resources. The largest extramural programs in health risk assessment research are at NIEHS and NCI; to a smaller extent, EPA's Research to Improve Health Risk Assessment program (RIHRA) funds university researchers (Adamson, 1992; Olden, 1992; Vandenberg, 1992).

The process for funding internal projects differs because the objectives of intramural research often differ from the objectives of extramural programs. An agency will support internal projects provided it has the expertise and the resources. Usually, internal projects are more closely tied to the agency's mission and are more limited in their scope.

A variety of funding mechanisms allow agencies to collaborate with other institutions and organizations on projects, sharing resources and avoiding any duplication of efforts. These mechanisms include memoranda of understanding between and among agencies and cooperative agreements to foster collaborations between the government and universities or private institutions. NIEHS, for example, has a memorandum of understanding with NIOSH for collaborative research in epidemiology and risk assessment of occupational hazards.

Targeting Risk Assessment Research

Agencies use targeted research to direct resources to areas of highest priority. In broad terms, targeted research is designed to solve a specific problem or meet an objective set in advance by an agency or by congressional imperative. In the context of this report, research can be targeted to areas likely to have the greatest impact on policy and decisionmaking. Targeted research is a tool that can be used to link research to the decisionmaking process.

Targeted research on health risks is especially appropriate for regulatory agencies that use risk assessment to develop standards, guidelines, and regulations. It is also appropriate for agencies like DOD and DOE that have research capability as well as an operational investment in the outcome of research-in the form of cleanup programs designed to reduce risk.

Targeted research is especially useful for filling gaps in the data required for specific risk assessments and, more generically, for developing new methods of performing risk assessment. It should not be confused with “mandated” or “manager-directed research, in which the scope and methods of a research project are dictated in advance by the managers of an agency. Such projects are less likely to undergo peer review and be awarded competitively.

Frequently people think of targeted research as synonymous with applied research, but targeted research can be either basic or applied, as long as its goal is to meet an agency’s established objective. The Human Genome Project of the NIH/DOE is an example of targeted research that is basic in orientation. As defined by OTA in this report, targeted research is linked to a specific goal; thus, terms such as “directed,” “identified,” or “prioritized” research are also appropriate. Any of those terms expands the concept of targeted research beyond the narrow connotation of applied research.

The most familiar method for Federal agencies to target research is Requests for Proposals issued to the scientific community to solicit research intended to address a specific problem. Scientists inside or outside the agency prepare competitive applications detailing how they would study the problem. After a process involving peer review and ranking of the proposals, funds are awarded to scientists whose applications appear most likely or best suited to yield an answer.

Only a few examples of targeted risk assessment research exist. (See ch. 7 for a discussion of

the features of successful research programs.) A small-scale model of targeted research is found in EPA’s RIHRA program (box 4-A). Another example of a targeted research program is emerging at FDA’s NCTR, where research proposals are now reviewed not only on the basis of scientific merit but also on the basis of relevance to the needs of the regulatory centers of FDA. (Previously, proposals were funded solely on the basis of scientific merit.) To ensure that regulatory relevance plays a role in proposal review, members of the reviewing committees are drawn from each center in FDA with regulatory responsibility (Norris, 1993).

DOE represents a case in which a targeted research program in health risk assessment would be useful to meet the challenge of environmental cleanup. DOE’s Office of Environmental Restoration and Waste Management is responsible for over \$5 billion in cleanup programs at DOE facilities in 1993. With the exception of the epidemiology program (under the Office of Epidemiology and Surveillance), DOE’s experimental toxicology effort is moving toward answering basic research questions related to molecular biology and the mechanisms of toxicity. Some point out that this shift toward basic research will improve the quality of DOE’s research and ultimately pay off in the applied arena. But others contend that valuable opportunities are being lost because research is not being targeted to the problems raised by the most costly cleanup effort ever undertaken by the Federal Government.¹²

FINDINGS AND CONCLUSIONS

To evaluate Federal research to improve health risk assessment, OTA used three distinct categories to classify health risk assessment research: 1) research to improve health risk assessment methodologies; 2) basic science and basic health risk research to understand how environmental agents produce their adverse effects and basic biological,

¹² For the first time in history, the cleanup costs for nuclear weapons facilities will exceed the cost of producing nuclear weapons.

Box 4-A—The Research To Improve Health Risk Assessment Program at EPA

The objective of EPA's Research to Improve Health Risk Assessments (RIHRA) program is to identify and conduct systematic, targeted research to improve the scientific basis and methods used in health risk assessment. In 1988, Congress mandated EPA to develop an integrated research program to reduce uncertainties in the risk assessment process. RIHRA is the agency's response to the environmental health risks aspects of the mandate.

RIHRA serves to complement other EPA research programs and address risk assessment issues facing the agency that cut across the regulatory programs. The program includes investigators from the Environmental Protection Agency's Health Effects Research **Laboratory** in its Office of Health Research; Office of Health and Environmental Assessment; and the Office of Modeling, Monitoring Systems, and Quality Assurance.

Projects are selected using defined criteria and awarded competitively. RIHRA's four major project areas include: 1) integrated exposure assessment; 2) physiologically based pharmacokinetic models; 3) biologically based dose-response models; and 4) analyses of uncertainty in risk assessment. Resources other than RIHRA funding are also used to support those areas of research at the agency.

EPA integrated RIHRA into its new research planning scheme, which is based on specific issues needing research support. This new issue-based planning places RIHRA under the Health Risk Assessment Methods issue. The major emphasis of this issue is scientific studies in the laboratory to support the development of predictive models for assessing health risks but also includes some chemical-specific assessments (e.g., dioxin). It is intended to complement the development of biological assays and chemical-specific data that is emphasized in other issues. Related research issues for RIHRA include the Health Effects issue, which emphasizes complementary development of data on the **way agents** produce adverse effects, and the Human Exposure issue, which provides information on the route, magnitude, frequency, and duration of exposures to environmental pollutants.

SOURCE: U.S. Environmental Protection Agency, Office of Research and Development, "Strategic Issue Plans" (April 1993).

physical, and chemical sciences; and 3) research to fill chemical-specific data gaps. OTA believes that progress must be made in all three areas to substantially improve the process of risk assessment and reduce the uncertainty of estimates of risk.

Taken as a whole, Federal research to improve risk assessment at the national level appears neither well integrated nor well planned. In particular, given the promise that methodological research offers, the resources allotted to it appear disproportionately small: in FY 1993, methodological research received approximately 11 percent of the estimated \$600 million spent on health risk assessment research. As a result, methodological research is a secondary priority for both research and regulatory agencies. In times of restricted resources and in the wake of congressional imperatives, the agencies tend to maintain their core programs and not

enter into new programs. Often, methodological research becomes marginalized as a consequence.

Yet expanding methodological research is not simply a matter of redirecting funds at the expense of either basic research or research on data collection. Instead, methodological research should be considered complementary to the other types of research that agencies are conducting and should be integrated into a complete research program. The results of basic research on biological processes and mechanisms of toxicity provide the biological framework for many of the methods and models being developed. Dose-response and pharmacokinetic models, for example, are based on information about physiology and metabolism obtained from basic research. Similarly, risk assessments benefit from research on data collection; a complete risk assessment requires data on toxicity, dose-response relationships, and exposures. Further-

more, methodological research, especially extrapolation models, and basic research are closely linked with chemical-specific data.

Charting a course for improving risk assessment research requires that Federal agencies work at several organizational levels. OTA examined the priority-setting process for such research at three different levels: national, agency, and program. Each level employs different processes and methods. Setting priorities at the program level involved the most formalized and systematic processes; the national level involved the least. In addition, several factors influence the choice of one type of research over another.

Despite the national implications of decisions based on risk assessment, Federal research to improve risk assessment is largely decentralized and uncoordinated. There is no central coordinating Federal presence. Most Federal research is done in support of the agencies and departments that sponsor the research, as is the case for environmental research and development in general (Carnegie Commission, 1992; Schaefer, 1991). OTA observed few multiagency efforts. An example is the FCCSET process, but participants and nonparticipants alike displayed little optimism about possible outcomes from it.

The absence of an identified central leader in risk assessment research contributes to the pessimistic viewpoint and to the current level of funding and disciplinary and agency fragmentation in the effort to improve health risk assessments. A nationally recognized leader could provide leadership and assurances about political support for research, promote multiagency collaborations, and provide incentives for overcoming bureaucratic hurdles and turf battles. A national leader in the White House in a position equivalent to the "Drug Czar" or "AIDS Czar," could bring national visibility and unify and coordinate research activities across agencies, in addition to articulating the needs of the field to Congress and the President. Furthermore, this central figure could instill a sense of common

purpose among researchers and program managers.

At the agency level, priorities are based on the different constituents, legislative mandates, and missions of the organizations. They are also influenced by historical factors and the composition of the work force, which gives rise to an agency culture that is important in determining how the organization establishes its directions and priorities. Often, political and public pressure dictate priorities to a greater extent than does a formal process within the agency (U.S. EPA, SAB, 1988).

The priorities for risk assessment research vary with the mission and function of the agency: specifically, whether the agency's responsibilities include risk management. The health regulatory agencies, DOD, and DOE conduct mostly chemical-specific data development, whereas the research agencies, by and large, conduct basic research.

Setting priorities at the program level is generally a more developed process—both more systematic and more formal—than it is at the agency or national levels. Generally, two distinct types of management methods are used to determine programmatic priorities for individual research projects (U.S. Congress, OTA, 1991). One style, termed "bottom-up," allows research ideas and priorities to originate with the individual researchers, who communicate those ideas to their superiors or to grant managers. In contrast, "top-down" management assigns priority-setting to the most senior decisionmakers in an agency. OTA observed both styles of management in its survey of risk assessment research, as well as a mixture of styles, which is consistent with federally funded science in general (U.S. Congress, OTA, 1991).

Risk assessment research has not kept abreast of the needs of our modern society. It is estimated that 1,500 new chemicals are introduced worldwide each year, which joins the more than 62,000 chemicals OTA estimates is already in use in the U.S. Studies suggest that only a fraction are

adequately, if at all, tested for toxicity. New insights from research can produce better tools to decide which chemicals require more investigation and which do not; which require regulation and which do not. Without better tools, governmental agencies and private companies will never catch upon the backlog of untested chemicals and unanswered questions, and the public will never have the assurance that sufficient research is being brought to bear on the risks that concern it.

CHAPTER 4 REFERENCES

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